

Fig. 22.1 T1 axial (a) and coronal (b) post-gadolinium-enhanced MRI showing multiple peripherally enhancing metastatic lesions in an individual with known metastatic breast cancer

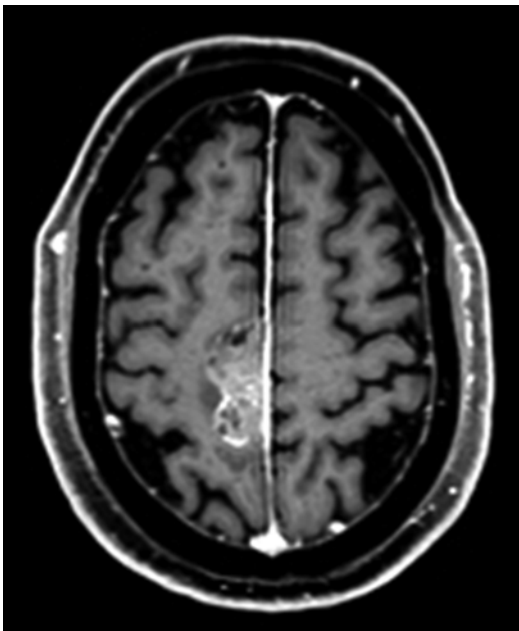


Fig. 22.2 T1 axial post-gadolinium-enhanced MRI showing a dural-based mass lesion along the right side of the falx, histologically confirmed to be a brain metastasis from prostate cancer

imaging showing leptomeningeal or subependymal enhancement. The diagnosis of leptomeningeal cancer is made when cerebrospinal fluid

cytology shows malignant cells, and/or characteristic neuroimaging features are present in the appropriate clinical context.

Primary Brain Tumors

Unlike brain metastasis, primary brain tumors arise from cells normally found in the brain (Fig. 22.4a). The overall incidence of primary brain tumors in adults is 21.03/100,000 [2]. Benign tumors are more common (10.5/100,000). Meningioma occurs more commonly in women, with an estimated incidence of 8.36/100,000 person-years in women compared to 3.61/100,000 in men [2]. The incidence increases with age and with estrogen supplementation. Additional risk factors include elevated body mass index, low self-rated physical activity levels, and a history of uterine fibroids [3]. Meningiomas are extra-axial, dural-based mass lesions that characteristically demonstrate avid homogeneous contrast enhancement (Fig. 22.4b), and are graded on a World Health Organization (WHO) scale from I to III depending on their histologic characteristics. Complete surgical removal, when possible, provides the greatest chance of cure.

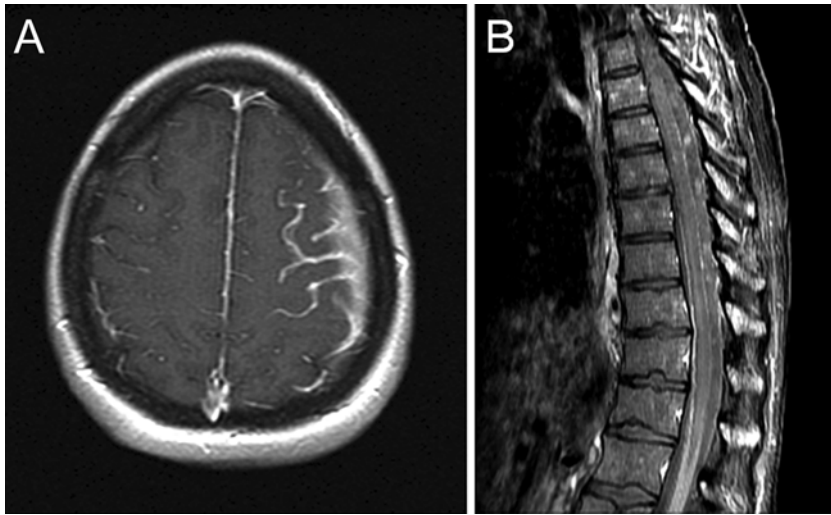


Fig. 22.3 Axial T1 post-contrast brain MRI (a) and sagittal post-contrast spine MRI (b) demonstrating abnormal leptomeningeal enhancement due to leptomeningeal metastasis

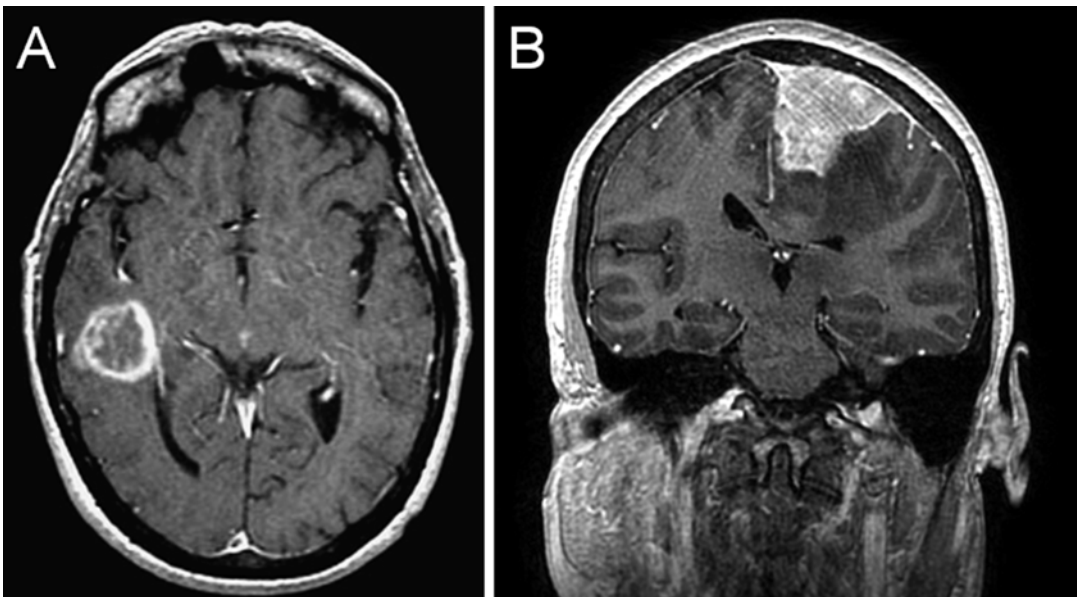


Fig. 22.4 T1 coronal post-gadolinium-enhanced MRI showing an intraaxial enhancing lesion, histologically confirmed to be a glioblastoma (a). T1 coronal post-

gadolinium-enhanced MRI showing a dural-based homogeneously enhancing lesion, histologically confirmed to be a meningioma (b)

Radiation therapy is an effective treatment for residual or recurrent disease, and is also important in the treatment of grade II and III tumors as these carry a higher risk of recurrence.

Gliomas are the most common malignant brain tumor in both adults and children, and represent 1.4 % of all new cancer cases diagnosed in the USA. They comprise 36 % of all brain and

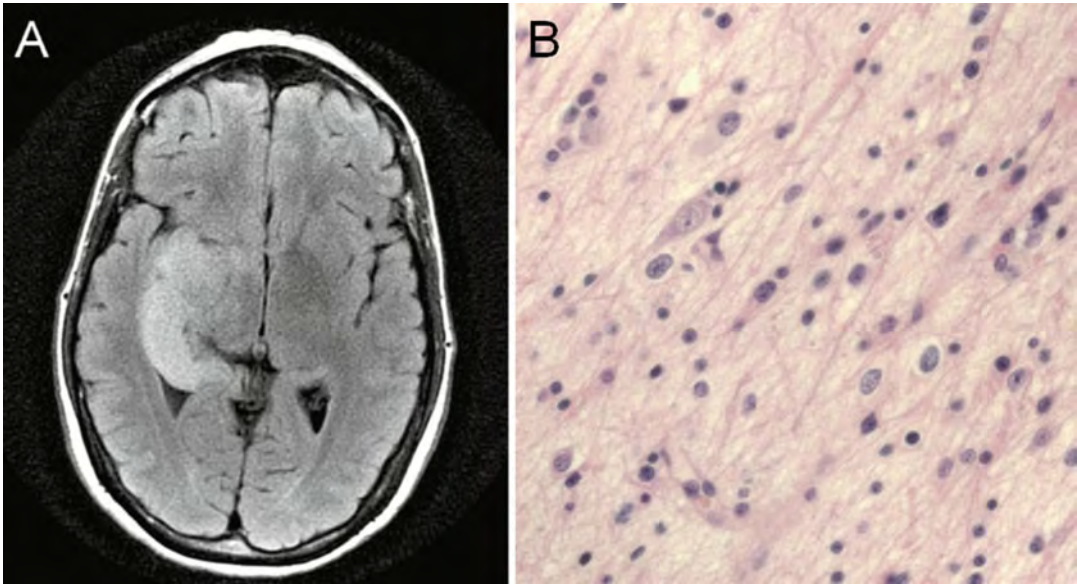


Fig. 22.5 T2 fluid-attenuated inversion recovery (FLAIR) MRI showing a T2 hyperintense, expansile abnormality in the right temporal lobe (a). Histologic analysis revealed a

grade II astrocytoma that showed increased cellularity, pleomorphism, and infiltration (b)

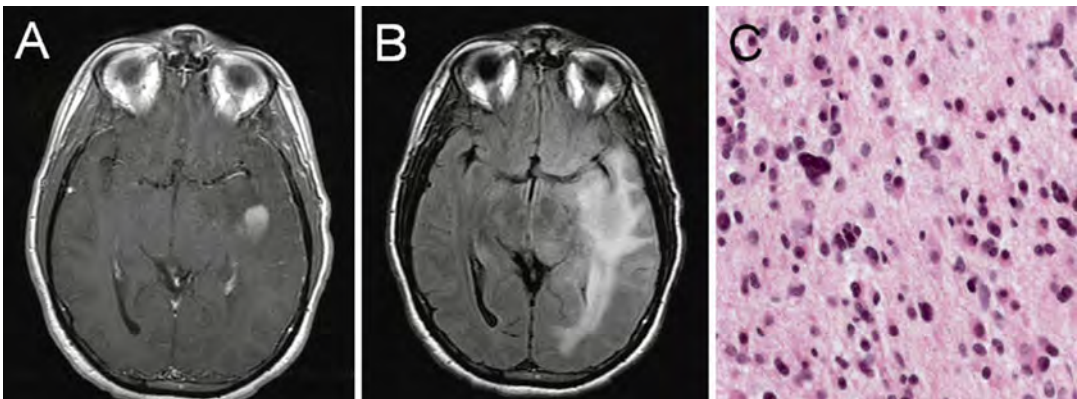


Fig. 22.6 T1 axial post-gadolinium-enhanced MRI (a) and T2 axial fluid-attenuated inversion recovery (b) images showing a left temporal anaplastic astrocytoma with a

central focus of homogeneous enhancement. Histologic analysis revealed a grade III astrocytoma that showed high cellularity, pleomorphism, and mitotic figures (c)

CNS tumors, and 81 % of all malignant brain tumors [2]. Gliomas are graded from WHO grades I to IV, with grades II (Fig. 22.5a, b) and III (Fig. 22.6a–c) characterized by increasing cellular atypia and anaplasia respectively, and WHO grade IV (Fig. 22.7a–e) demonstrating vascular proliferation and necrosis. Medulloblastoma

(Fig. 22.8a, b), ependymoma (WHO grades II–III) (Fig. 22.8c), pilocytic astrocytoma (WHO grade I) (Fig. 22.8d), and diffuse infiltrative pontine glioma (WHO grade II) (Fig. 22.8e) are more often seen in children, while glioblastoma (WHO grade IV) is the most common malignant brain tumor in adults.

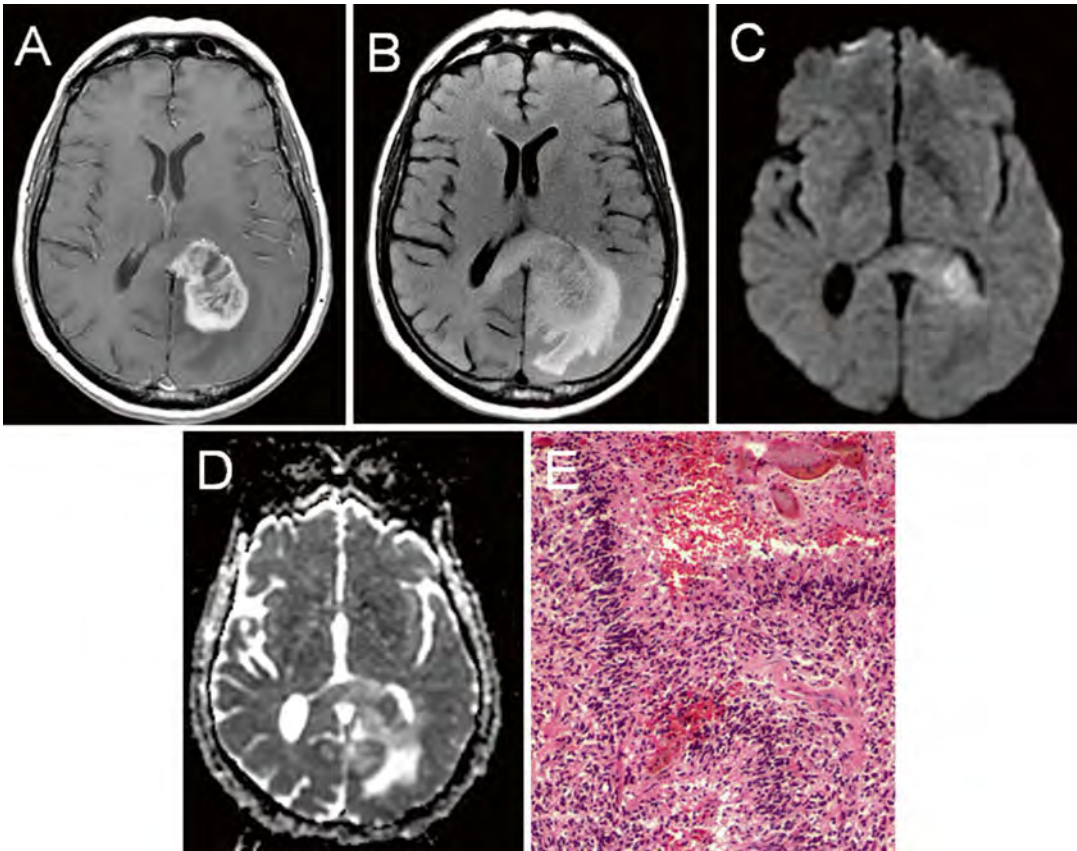


Fig. 22.7 T1 axial post-gadolinium (a), T2 FLAIR (b), diffusion-weighted imaging (c), and apparent diffusion coefficient (d) imaging of a left-hemisphere glioblastoma. The peripheral enhancing pattern and nonenhancing expansile changes crossing the midline via the corpus callosum are

characteristic. DWI (c) and ADC (d) imaging reveal an area of diffusion restriction consistent with increased cellular density in the region. Histologic analysis revealed a grade IV glioblastoma that showed high cellularity, pleomorphism, microvascular proliferation, and necrosis (e)

Classification and Grading

Unlike systemic cancer, staging is not undertaken for primary brain tumors, and spread of systemic malignancy to the CNS would qualify as stage IV disease. However, an extent of disease evaluation in known or suspected CNS malignancies such as CNS lymphoma or brain metastasis presenting when the status of systemic disease is unknown is important. Spine imaging in known or suspected leptomeningeal cancer, especially if there are signs or symptoms of nerve root involvement, is also appropriate.

CNS tumors are traditionally graded upon acquisition of tumor tissue based on histologic appearance. The World Health Organization (WHO) Classification of Central Nervous System

Tumors is the most widely accepted histologic grading system [4]. It classifies tumors based on histopathologic and immunohistochemical features, and is revised periodically to reflect advances in the field based on expert consensus. In the WHO classification, grade I and II tumors are designated as low grade, and grade I tumors are considered potentially curable with surgery. Grade III and IV tumors are high grade, with more aggressive growth potential. They often require radiation and/or chemotherapy in addition to surgical resection.

In some tumors, better understanding of the genetic abnormalities in the tumor has led to advances in molecular phenotyping. The Cancer Genome Atlas (TCGA) project, for example, completed genomic sequencing of 206 glioblastomas [5]. TCGA provided new insights into the

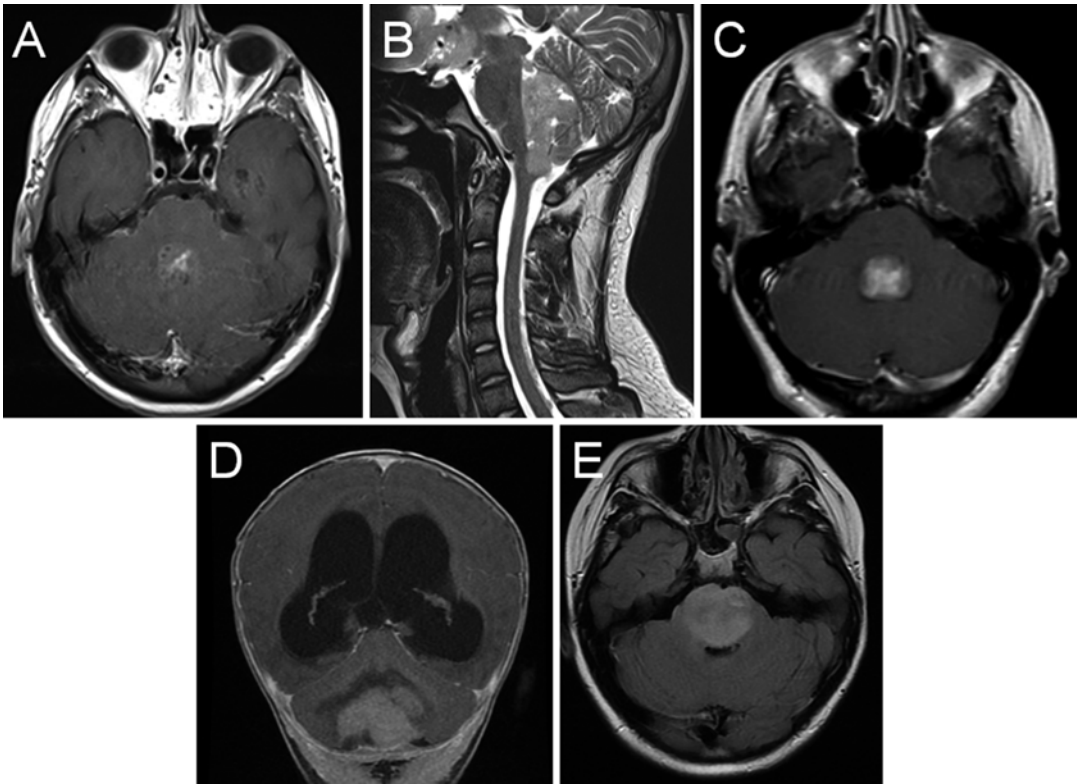


Fig. 22.8 Axial T1 post-gadolinium (a), and sagittal T2 (b) MRI showing a posterior fossa mass lesion with an enhancing component. Surgical resection revealed a medulloblastoma. Axial T1 post-gadolinium (c) shows a

fourth ventricular ependymoma. Coronal T1 post-gadolinium (d) shows a cerebellar pilocytic astrocytoma with obstructive hydrocephalus. Axial FLAIR (e) shows a diffuse infiltrative pontine glioma

frequency of specific genetic abnormalities in glioblastoma. The information from TCGA led to a proposed classification scheme in which four distinct molecular phenotypes in glioblastoma were derived by consensus clustering based on abnormalities in platelet-derived growth factor receptor (PDGFR)-A, isocitrate dehydrogenase (IDH)-1, epidermal growth factor receptor (EGFR), and neurofibromatosis (NF)-1 [6].

The four molecular phenotypes are designated classical, mesenchymal, neural, and proneural. The classical glioblastoma subtype is characterized by chromosome 7 amplification paired with chromosome 10 loss. There was also a higher frequency of EGFR amplification, and less frequent TP53 mutation than other GBM subtypes. The mesenchymal subtype was characterized by focal deletions of a region of chromosome 17 that contains the NF1 gene, and high expression of genes in the tumor necrosis factor and NF-kappa

B pathways. The neural subtype showed prominent expression of neural markers.

The proneural subtype demonstrated amplification and increased gene expression of PDGFRα and a higher frequency of point mutation in IDH-1 than other subtypes. Proneural classification was somewhat less common, associated with younger age at onset and a tendency toward better overall survival than other GBM subtypes. When the molecular phenotyping was expanded to include analysis of histologic grade II and III gliomas, a number of lower grade gliomas were found to have a proneural molecular signature. These were characterized by the coexistence of IDH1 mutation and CpG island methylator phenotype (CIMP). Codeletion of chromosomes 1p and 19q, long identified as a favorable prognostic feature in oligodendroglial tumors, was found in many grade II and III tumors as well. The combination of IDH-1 mutation/CIMP+ and 1p;19q

codeleted molecular signature predicted longer survival when compared to IDH-1 wild-type/CIMP- and 1p;19q non-deleted tumors independent of tumor histology [7].

DNA repair is one mechanism of resistance to chemoradiation in high-grade gliomas. The most common chemotherapeutic agent for glioblastoma, temozolomide, is an alkylating agent with good CNS penetration that acts by methylation of guanine at the O-6 position. Methylation disrupts DNA replication and ultimately leads to apoptosis. The DNA repair enzyme methylguanine methyltransferase, or MGMT, reverses the methylation activity of temozolomide. High-grade gliomas that have a methylated (inactive) MGMT promoter show prolonged median overall survival and improved 2-year survival with concurrent radiation and temozolomide chemotherapy plus adjuvant monthly temozolomide. Tumors with an unmethylated (active) MGMT promoter region have no significant benefit from treatment with alkylating chemotherapy [8]. MGMT promoter methylation is associated with the CIMP phenotype found most commonly in the proneural glioma subtype. Strategies to inactivate the DNA repair activity of MGMT or administer a chemotherapy that is not dependent on DNA methylation are potential strategies to improve outcomes in individuals with MGMT unmethylated tumors.

A more detailed understanding of molecular phenotyping will continue to provide insight into differences in the biologic behavior among malignant glioma subtypes, as well as differences in survival and response to treatment with chemotherapy. Identifying important molecular pathways also provides potential targets for future therapies.

Advances in Diagnosis

Molecular Diagnostic Tools

As the field of cancer genomics provides new insight into specific genetic alterations that characterize CNS cancers, better tests are being devised that achieve less invasive and potentially earlier detection, improve diagnostic certainty,

and will give information about prognosis, or one or more specific therapeutic targets.

Cerebrospinal fluid (CSF) analysis is a diagnostic test that, if successful, may provide information to guide treatment without requiring craniotomy. This approach would be especially important for mass lesions that are in areas that are high risk to biopsy. Historically, the main CSF diagnostic tools are CSF cytology, flow cytometry, and a handful of molecular tests including CSF lactate dehydrogenase, beta-2-microglobulin, and Epstein-Barr virus DNA by polymerase chain reaction (PCR). Unfortunately, all of these tests are limited by low sensitivity or specificity.

More recently, proteomics and micro-RNA analysis of cerebrospinal fluid has emerged with the potential to differentiate lymphoma from other CNS inflammatory disorders, and potentially improve the detection of solid tumor CSF spread as well (Fig. 22.9a–c). Compared to conventional cytology, which had a sensitivity of 17 %, elevated levels of proteins associated with B-cell proliferation and migration (interleukin-10 and chemokine CXCL-13) in combination were shown to be 54 % sensitive and 99 % specific in the detection of CNS lymphoma [9]. Elevations in a combination of three specific micro-RNA levels from CSF in individuals with primary CNS lymphoma were 95.7 % sensitive and 96.7 % specific compared to controls [10]. CSF micro-RNAs in the diagnosis of glioma have a 90 % sensitivity and 100 % specificity to identify glioma compared to controls [11]. Micro-RNA levels in CSF have been used to successfully differentiate cancer from nonneoplastic brain lesions, and in some cases to distinguish metastasis from lung cancer versus breast cancer [12]. In solid tumors, elevated levels of CSF vascular endothelial growth factor (VEGF) had 75 % sensitivity, 97 % specificity, and 94 % negative predictive value in the diagnosis of breast cancer leptomeningeal metastasis compared to CSF cytology [13].

Circulating Tumor Cell Detection

Over the past 5–10 years, it has become possible to isolate circulating tumor cells (CTCs) in whole blood. Cells are obtained by using markers to

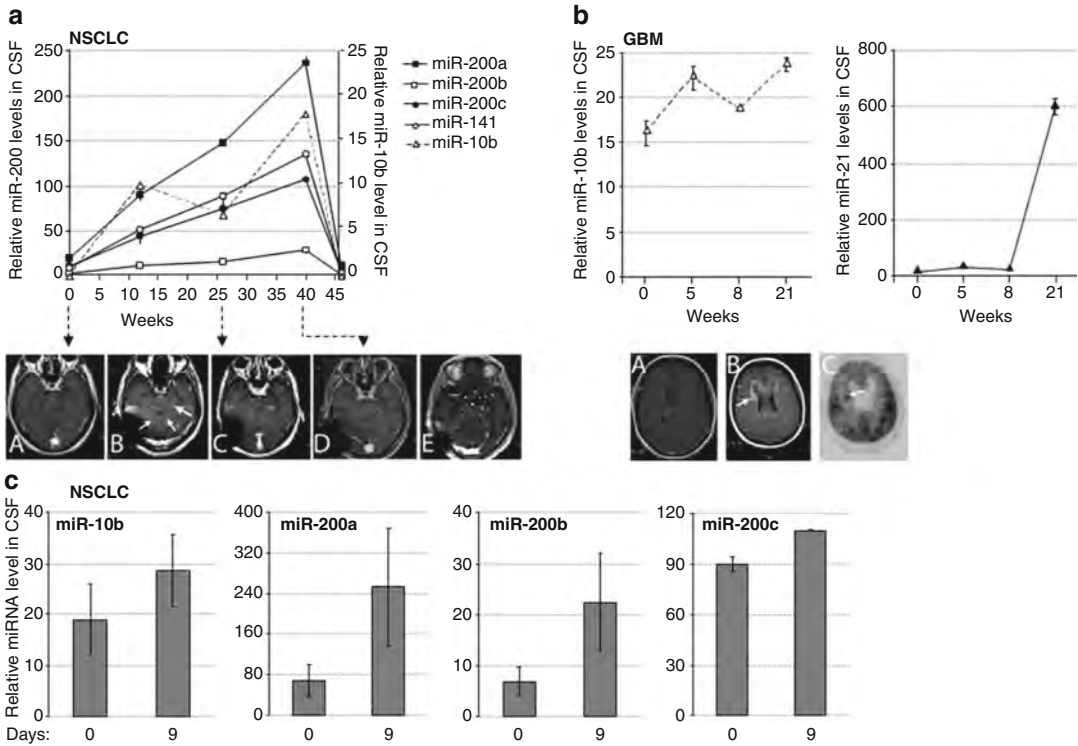


Fig. 22.9 The CSF levels of miRNA markers in metastatic lung cancer and GBM patients during treatment with erlotinib. miRNA levels were examined by qRT-PCR in CSF samples of lung cancer patients (**a**, **c**) and GBM patient (**b**) during the time course of erlotinib treatment. The disease progression and the drug response were concomitantly monitored by MRI, as follows. For Patient A: serial axial post-gadolinium MRIs of lung cancer patient's brain during course of progression of disease and stability and improvement on MRI with escalating doses of erlotinib. (A) Time 0 weeks while patient on erlotinib, there is no leptomeningeal and parenchymal enhancement and CSF cytology was negative; (B) 3 weeks progression on erlotinib 150 mg daily dosing with new cerebellar leptomeningeal enhancement (*small arrows*) and nodule (*large arrow*), erlotinib increased to 600 mg every 4 days at 9 weeks; (C) 29 weeks on showing stable leptomeningeal enhancement and nodule; (D) 40 weeks showing reduction in leptomeningeal enhancement and nodule, erlotinib increased to 900 mg every 4 days at 41 weeks; (E) 64

weeks after six cycles of chemotherapy with carboplatinum and pemetrexed due to lung cancer progression showing further reduction in leptomeningeal enhancement and nodule has disappeared. For Patient B: (A) time 2 weeks for patient with recurrent GBM with prominent mass effect and enhancement felt to be radiation changes rather than tumor based on MRI spectroscopy and FDG-PET scan on erlotinib at 600 mg every 4 days; (B) 26 weeks on treatment showing progression on MRI with new lesion (*arrow*) concerning for tumor; (C) 27 weeks on treatment showing hypermetabolic area (*arrow*) on PET consistent with tumor and biopsy confirmed. For Patient C: Had inadequate treatment due to functional status and rapidly progressed over a few weeks, which was reflected by an increase in levels of miR-200 family members in a short interval. (All: Reproduced with permission from Teplyuk NM, Mollenhauer B, Gabriely G, Giese A, Kim E, Smolsky M et al. MicroRNAs in cerebrospinal fluid identify glioblastoma and metastatic brain cancers and reflect disease activity. *Neuro-oncology* 2012;14(6):689–700)

detect epithelial cell adhesion molecules that are present on tumor cells, but not expressed on normal blood cells. The same technology used in whole blood may be used with CSF, and live tumor cells can be isolated this way [14, 15]. The clinical significance of asymptomatic CTCs in cerebrospinal fluid, and the reliability of following CTC counts

as a marker of response to therapy as an adjunct or in lieu of cytology, remains to be determined. It is possible that CTC technology will allow considerably earlier detection of CNS involvement. Earlier detection and initiation of CNS-directed therapies may positively impact survival outcomes in brain and leptomeningeal metastasis.

Neuroimaging

Contrast-enhanced magnetic resonance imaging (MRI) is the diagnostic test of choice for identification and characterization of brain tumors (Fig. 22.1a, b through 22.8a–e, Figs. 22.10a–c, 22.11, 22.12a, b). Among other advantages, increases in field strength from 1.5 to 3 T scanners for clinical use have resulted in greater distinction between contrast-enhancing and non-enhancing regions, improved spatial resolution, and more clear differentiation of tissue types (spectral resolution). Perfusion-weighted imaging and assessment of relative cerebral blood volume to identify areas of hyperperfusion make it possible to more accurately discriminate between neoplastic and inflammatory brain lesions or subacute infarction (Fig. 22.12a, b).

Imaging assessment following radiation therapy for brain tumors presents a potential challenge. Increases in the volume of abnormal enhancement and surrounding T2 hyperintensity may be seen with tumor progression or treatment effect from radiation. Distinguishing between the two based on neuroimaging can be

difficult or sometimes impossible. Radiographic assessment of tumor progression or response to treatment was traditionally performed using MacDonald criteria [16]. More recently, the Response Assessment in Neuro-Oncology (RANO) working group created modified criteria that account for the confounding effects of radiation therapy and anti-angiogenic treatments (Table 22.1) [17]. The RANO criteria provide a standardized approach to response assessment in brain tumors, which is useful for clinical trials and to avoid inaccuracies in imaging interpretation. To account for the potential confounding effects of radiation therapy on imaging, RANO criteria specify that increased volume of enhancing abnormality within the first 12 weeks following radiation therapy will not qualify as progression without tissue confirmation of active tumor or evidence of growth outside the radiation field. Additionally, RANO differs from MacDonald criteria in that progression of disease may occur with an increase in the volume of the nonenhancing T2 abnormality, or with clinical worsening that occurs without an alternate explanation.

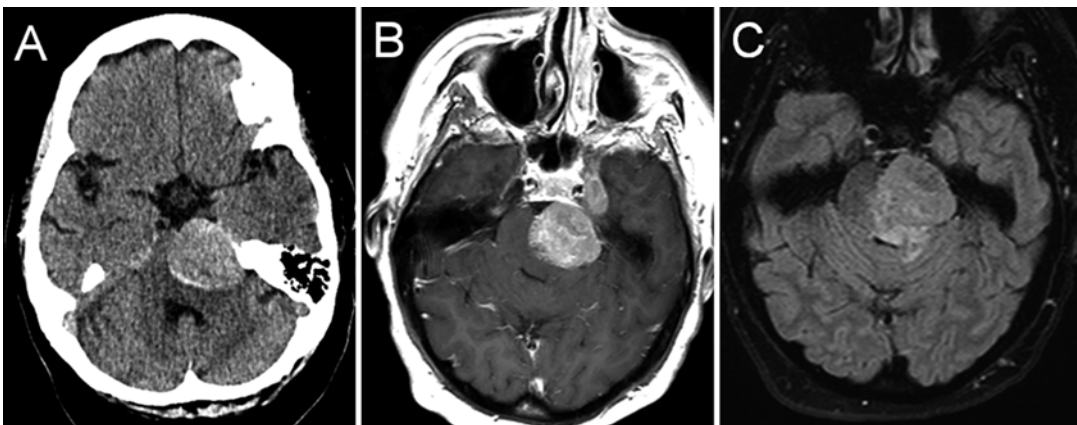


Fig. 22.10 Radiographic features of CNS melanoma. Axial non-contrast head CT shows a hyperdense mass lesion on the left displacing the pons (a). Axial T1-weighted

MRI with contrast demonstrates homogeneous contrast enhancement (b), and axial T2 FLAIR (c) at the same level demonstrates an expansile T2 hyperintense lesion

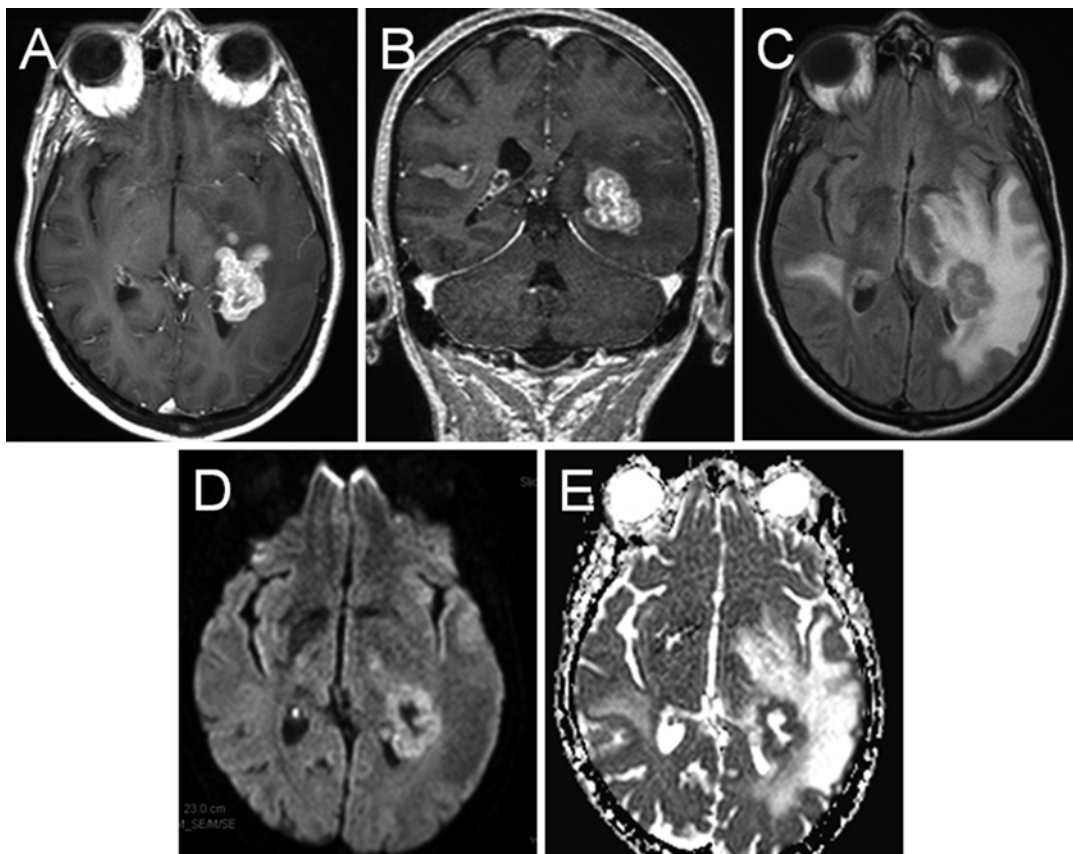


Fig. 22.11 MRI characteristics of diffuse large B-cell lymphoma. T1-weighted axial (a) and coronal (b) post-contrast imaging reveals an avidly contrast-enhancing mass lesion in the deep white matter with extension into

the lateral ventricle on the *left*. There is a substantial amount of vasogenic edema surrounding the lesion (c), and restricted diffusion of water seen on DWI (d) and ADC (e)

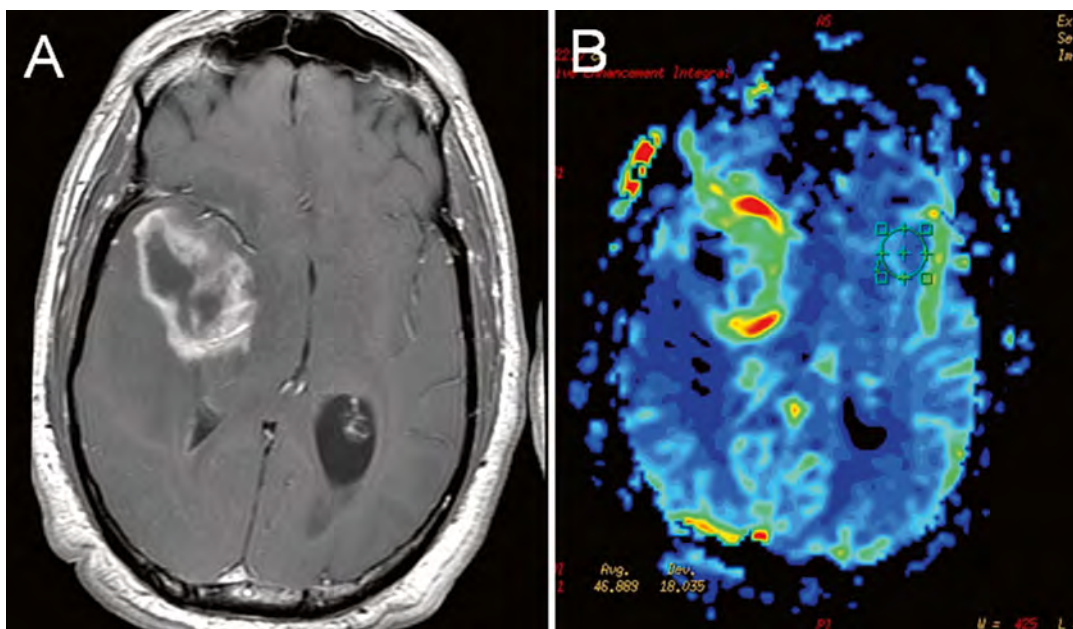


Fig. 22.12 Axial T1 post-gadolinium (a) and perfusion (b) MRI showing areas of increased cerebral blood volume corresponding to areas of contrast enhancement within a right frontal lobe glioblastoma

Table 22.1 A comparison of the MacDonald versus RANO criteria for the radiographic assessment of response to therapy in malignant glioma

	MacDonald criteria [16]	Response Assessment in Neuro-Oncology (RANO) criteria [17]
<i>Complete response (CR)</i>	<i>All of the following:</i>	<i>All of the following:</i>
MRI T1-post-Gd	Disappearance of all enhancing tumor on consecutive CT or MRI scans at least 1 month apart	Complete disappearance of all enhancing measurable and nonmeasurable disease sustained for at least 4 weeks; no new lesions
MRI T2/FLAIR	–	Stable or improved nonenhancing (T2/FLAIR) lesions
Corticosteroid	Off steroids	Off corticosteroids (or on physiologic replacement only)
Clinical	Neurologically stable or improved	Stable or improved clinically
<i>Partial response (PR)</i>	<i>All of the following:</i>	<i>All of the following:</i>
MRI T1-post-Gd	≥50 % reduction in size of enhancing tumor on consecutive CT or MRI scans at least 1 month apart	≥50 % decrease compared with baseline in the sum products of perpendicular diameters of all measurable enhancing lesions sustained for at least 4 weeks; no progression of nonmeasurable disease; no new lesions
MRI T2/FLAIR	–	Stable or improved nonenhancing (T2/FLAIR) lesions on same or lower dose of corticosteroids compared with baseline scan
Corticosteroid	Steroids stable or reduced	Steroid dose no greater than the baseline scan dose
Clinical	Neurologically stable or improved	Stable or improved clinically
<i>Progressive disease (PD)</i>	<i>Any of the following:</i>	<i>≥12 weeks after completion of chemoradiotherapy, any of the following:</i>
MRI T1-post-Gd	≥25 % increase in size of enhancing tumor or any new tumor on CT or MRI scans	<12 weeks after completion of chemoradiotherapy Only if there is new enhancement outside of the radiation field (beyond the high-dose region or 80 % isodense line) or if there is unequivocal evidence of viable tumor on histopathologic sampling

(continued)

Table 22.1 (continued)

	MacDonald criteria [16]	Response Assessment in Neuro-Oncology (RANO) criteria [17]	
MRI T2/FLAIR	–	Significant increase in T2/FLAIR nonenhancing lesion	
Corticosteroid	Steroids stable or increased	Stable or increasing doses of corticosteroids	
Clinical	Or neurological worsening	Clear clinical deterioration not attributable to other causes apart from the tumor (e.g., seizures, medication adverse events, complications of therapy, cerebrovascular events, infection) or changes in corticosteroid dose; failure to return for evaluation as a result of death or deteriorating condition	Insufficient to determine progression in the period < 12 weeks after completion of chemoradiotherapy given the potential impact of radiation treatment effect
<i>Stable disease</i> (SD)	“All other situations”	All of the following:	
MRI T1-post-Gd		Does not qualify for complete response, partial response, or progression	
MRI T2/FLAIR		Stable nonenhancing (T2/FLAIR) lesions on same or lower dose of corticosteroid compared with baseline scan	
Corticosteroid		In the event that the corticosteroid dose was increased for new symptoms and signs without confirmation of disease progression on neuroimaging, and subsequent follow-up imaging shows that this increase in corticosteroids was required because of disease progression, the last scan considered to show that stable disease will be the scan obtained when the corticosteroid dose was equivalent to the baseline dose	
Clinical		Stable or improved clinically	

Advances in Therapy

Surgery

Cytoreduction via maximal safe surgical resection is an extremely important part of treatment for gliomas. The extent of resection has been shown to impact survival, especially in low-grade glioma [18], but also in retrospective series of grade III and IV gliomas [19]. Advances such as intraoperative MRI and fluorescence-guided resection have been investigated as potential ways to achieve more complete resection.

Intraoperative imaging has been employed by brain tumor surgeons in tertiary care centers (Fig. 22.13a–c). In some series, the real-time assessment of extent of resection has impacted surgical planning, and has made it possible to achieve more complete surgical resection of brain tumors compared to preoperative MRI and direct visualization during surgery. Some have combined intraoperative MRI with awake craniotomy and functional brain mapping. Further evaluation is needed to determine whether the added resources, surgical time, and demand on the patient result in an impact on survival or functional outcomes.

In gliomas, the extent of infiltrating (nonenhancing) tumor can be difficult to determine on preoperative imaging, and so techniques that

employ fluorescent labeling of tumor cells are of potential utility. Improved visualization of residual tumor and less residual tumor following surgery were achieved with presurgical administration of 5-aminolevulinic acid-induced porphyrins and intraoperative fluorescence compared to conventional neuronavigation [20]. Prolonged survival was also observed in those who had no residual fluorescence following surgery. More recently, other tumor markers have been employed such as chlorotoxin conjugated with indocyanine green for visualization in the near-infrared spectrum [21]. For high-grade gliomas, additional treatment with chemotherapy and/or radiation is required to prolong survival and delay growth of the tumor.

Angiogenesis Inhibition

Vascular proliferation has long been identified as a hallmark of cancer, and is especially prominent in high-grade gliomas. Bevacizumab, a humanized monoclonal antibody to circulating vascular endothelial growth factor (VEGF), was approved by the US Food and Drug Administration for treatment of recurrent high-grade glioma in 2010. Bevacizumab treatment at recurrence resulted in a 6-month overall survival of 77 %, and 57 % with at least a partial radiographic response on imaging [22].

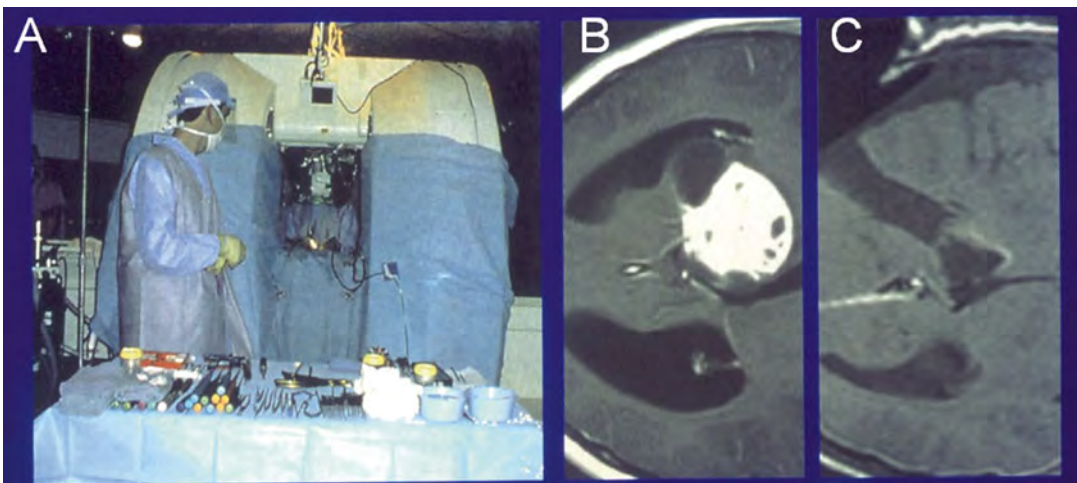


Fig. 22.13 Intraoperative MRI (a) can be used to obtain better extent of resection safely. Preoperative axial T1 post-gadolinium MRI shows a large deep thalamic tumor (b), which was totally resected under guidance of intraoperative MRI (c)

Phase III studies of bevacizumab in addition to standard chemoradiation with temozolomide for treatment of glioblastoma in the up-front setting are ongoing. In addition to monoclonal antibody therapy, receptor tyrosine kinase inhibitors targeting multiple receptors involved in angiogenesis and cellular growth and proliferation have been studied with limited impact on survival.

Vaccine-Based Therapies

The interplay between the immune system and cancer is an area of ongoing interest in glioma biology. As more is understood, vaccine-based therapies have been created that show T-cell responses to tumor antigens, and in some instances have resulted in increased overall survival compared to matched controls. The epidermal growth factor receptor (EGFR) vIII mutation is not found in normal tissue, but is present in approximately 1/3 of glioblastomas. A vaccine to EGFR vIII administered to 18 glioblastoma patients showed that among those who showed evidence of mounting an antibody response, the median overall survival was 47.7 months, compared to 22.8 months who did not mount a response and 15 months for the control group [23]. Another approach to vaccine therapy is the development of dendritic cell vaccines using the patient's own serum and cell lines cultured from their own tumor tissue to create vaccines to tumor-associated antigens. This approach allows for targeting of multiple patient-specific tumor antigens, including those expressed on glioma stem cells, with the goal of inciting an immune response against the tumor [24].

Virus-Based Therapies

Viruses have been of interest in brain tumor therapy because of their ability to transfect tumor cells. Most virus therapies are injected directly into the tumor bed at the time of surgery. Delivery may also be accomplished with stereotactic guidance or convection-enhanced delivery. Intravenous administration of virus is being studied. There are a number

of mechanisms by which viruses may be used therapeutically. Oncolytic viruses infect tumor cells, and cause direct damage or apoptosis. Enzyme/prodrug therapy is a mechanism by which a virus delivers a prodrug to the tumor that is subsequently activated. Viral gene transfer is a third mechanism in which normal genes are delivered to the tumor using viral vectors with the goal of restoring normal function of specific genetic pathways such as TP53 [25]. Ongoing early clinical trials and combining virus therapies with immunotherapy or radiation hold promise to provide better treatment options in glioma as well as brain metastasis.

Tumor Treating Fields

Regional therapy with a device that delivers alternating electrical fields (200 kHz) to disrupt cell division has been studied in recurrent glioblastoma, and is currently under investigation for up-front therapy and in brain metastasis. The Tumor Treating Fields (TTFields) (Optune™, Novocure, Ltd, Haifa, Israel) device is an electrode array that is configured based on the tumor location, and delivers alternating electrical fields to the tumor bed intended to selectively disrupt the process of cell division (Fig. 22.14). In the recurrent setting, TTFields demonstrated non-inferiority to chemotherapy, without hematologic side effects or interactions with other chemotherapies [26]. More recently, a planned



Fig. 22.14 Novo-TTF portable device with battery pack and scalp electrodes (Copyright © 2014 Novocure. All Rights Reserved)

interim analyses from a randomized phase 3 trial of TTFields plus temozolomide in patients with newly diagnosed glioblastoma showed significantly increased progression-free survival and overall survival compared with standard therapy (temozolomide) alone. Systemic toxicity did not increase with addition of TTFields therapy to temozolomide [27].

Radiosurgery

Advances in radiosurgical technique and image guidance have led to the ability to deliver high-dose radiation to areas that would previously be treated with conventional fractionated radiotherapy. As more is learned about the detrimental long-term neurocognitive effects of whole-brain irradiation, stereotactic radiosurgery is often considered as an alternative to whole-brain irradiation in the treatment of brain metastasis [28].

Conclusions

The future of neuro-oncology is promising on a number of new frontiers. More sensitive diagnostic modalities will improve accuracy and provide a less invasive means to establish a diagnosis. Better classification and characterization of tumors based on genetic features will more accurately predict prognosis and response to treatment. A better understanding of tumor stem cells and immunology has provided new therapeutic targets and modes of treatment delivery, many of which are being studied in clinical trials. In virtually all aspects, advances in the basic and clinical sciences have impacted care and contributed to new therapies for individuals with brain tumors.

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CHAPTER 17

Tumor-Treating Electric Fields for Glioblastoma

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HISTORICAL CONTEXT OF ELECTRIC FIELD TREATMENT

The application of physical energy from various parts of the electromagnetic spectrum is common in glioblastoma treatment. The most widely used involves energies from the higher end of the spectrum in exahertz (the 10^{18} -Hz range), in which ionizing radiation is used to treat various types of malignancies, including glioblastoma (Fig. 17.1). Therapeutic radiation can be diffuse, as in whole-brain and involved-field radiotherapy, or highly conformal, as in stereotactic radiosurgery (SRS), and the biological responses to these different types of radiation are different, as modeled by the linear-quadratic dose-effect relationship.¹⁻³ At the lower end of the spectrum, in the gigahertz or 10^9 -Hz microwave range, laser interstitial thermal therapy (LITT) is being used for the thermocoagulation of brain tumors and the treatment of radiation necrosis.⁴⁻⁶ MRI technology now allows the real-time visualization of temperature changes during LITT treatment of a target lesion. In addition, at an even lower part of the electromagnetic spectrum, in the kilohertz or 10^3 -Hz range, alternating electric field therapy or tumor-treating electric fields (TTFields) are now an established treatment for glioblastoma.⁷ This chapter provides a summary of the cell biology and physical science effects of TTFields on tumor cells and tumors in the brain, as well as a historical perspective of the clinical studies conducted in the glioblastoma population.

BIOLOGICAL BASIS AND PHYSICAL SCIENCE SUPPORTING THE USE OF TUMOR-TREATING ELECTRIC FIELDS

Cell Biology Effects of Tumor-treating Fields

Early *in vitro* studies showed that cells exposed to TTFields underwent violent membrane blebbing during mitosis, thought to be a result of the disruption of alpha/beta tubulin assembly in mitotic spindles.^{8,9} More detailed analysis revealed that these cells seem to transit normally through metaphase, showing normal rates of cyclin B destruction and metaphase exit at times consistent with the expected entry into anaphase.¹⁰ However, anaphase and cytokinesis were perturbed, leading to aberrant mitotic exit. Mitosis is dominated by a myriad of processes that must be regulated spatially and temporally in order to ensure even distribution of parental genomic DNA into the resulting daughter cells. Most of the regulatory events during mitosis control functions that are involved in the migration and alignment of chromosomes, as well as the timing of the contraction of the cytokinetic furrow following chromosome separation. Given the timing of the TTField-induced cellular disruption during mitosis, they likely exert their effect on intracellular proteins that are necessary during late metaphase or anaphase and that bear high electric charges on which the TTFields can act. It is not clear whether these TTField effects are caused by their combined activities on multiple proteins or whether they arise from the perturbation of a single protein that serves a critical function. In order to serve as a TTField target,

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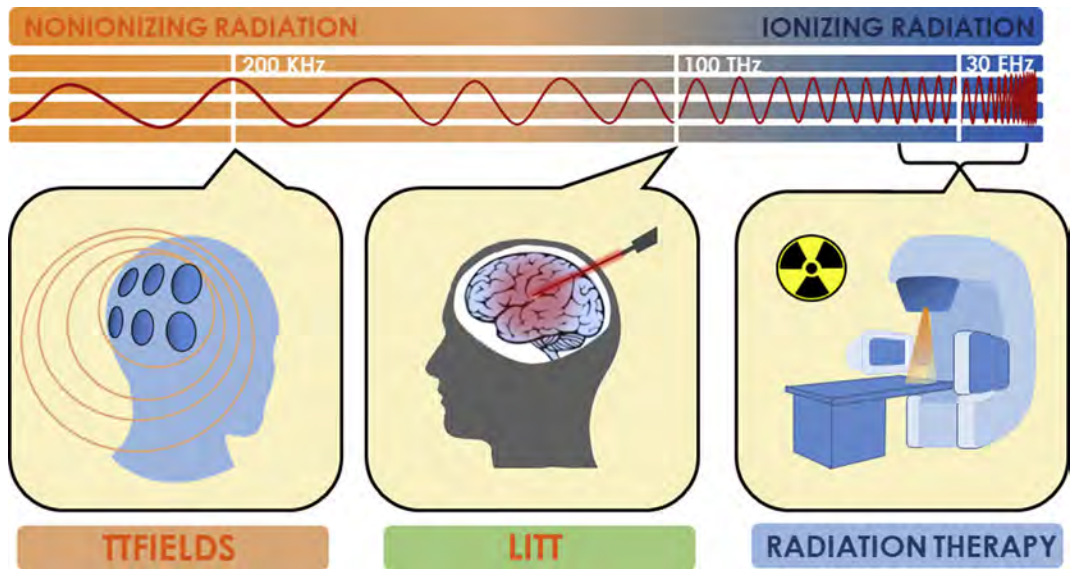


Fig. 17.1 Application of the electromagnetic spectrum in the treatment of brain tumors. Traditional ionizing radiation has a frequency in the exahertz, or 10^{18} Hz, range, whereas laser-induced thermal therapy uses microwaves in the gigahertz, or 10^9 Hz, range to induce thermocoagulation. Tumor-treating electric fields use the lower end of the electromagnetic spectrum in the kilohertz, or 10^3 Hz, range. LITT, laser interstitial thermal therapy; TTFIELDS, tumor-treating fields. (Courtesy of Kisa Zhang, BS, Boston, MA.)

proteins must possess a sufficiently high dipole moment in order for the alternating electric fields generated by the TTFIELD therapy device to perturb its function in mitosis.

By examining the published dipole moment database of different proteins, the authors found that the heterotrimeric protein complex composed of septin 2, 6, and 7 possesses a dipole moment of 2711 Debyes (or 10^{-18} statC·cm SI equivalent), which is 5 standard deviations greater than the median value derived from an analysis of more than 14,000 intracellular proteins.^{10,11}

Importantly, this septin complex performs important functions during both metaphase and anaphase and its disruption by short hairpin RNA-mediated depletion resulted in blebbing during mitosis similar to that seen in TTFIELD-treated cells.¹² TTFIELDS are able to perturb normal septin localization during mitosis and cell spreading, which strongly suggests that TTFIELDS physically interact with this complex and exert their effects on mitotic cells by preventing the proper localization of this septin-containing complex to proper sites of action during mitosis (Fig. 17.2).

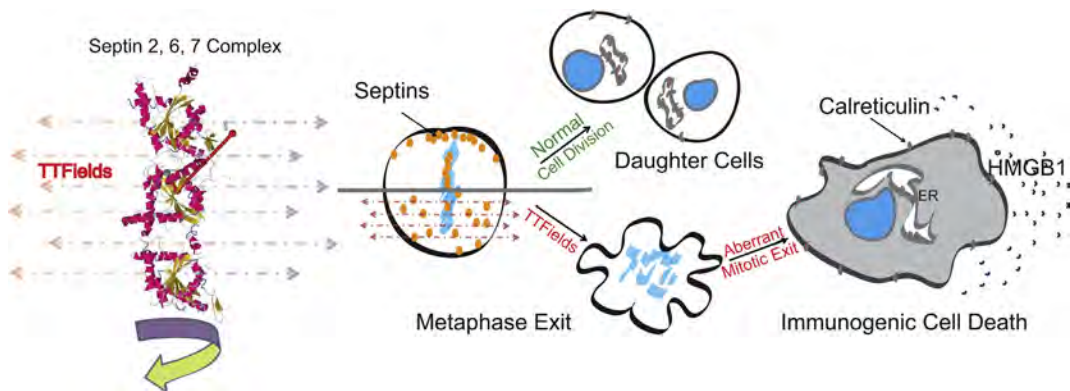


Fig. 17.2 Interaction between TTFIELDS and tumor cells undergoing mitosis. TTFIELDS induce an electromechanical force on the septin 2, 6, and 7 complex that has an extremely large dipole moment of 2711 Debyes. This movement results in mitotic catastrophe and aberrant mitotic exit, leading to an increased cell surface expression of the endoplasmic reticulum chaperonin calreticulin and the secretion of HMGB1, which acts as a danger signal when released from cells, both of which are essential for immunogenic cell death.

The TTFIELD-induced catastrophe during anaphase results in a failure to complete division that results in a G₀/G₁ arrest and p53-dependent apoptosis. Therefore, TTFIELDS are likely to exert an effect on multiple proteins and the resulting cumulative perturbation may be necessary to drive the observed mitotic catastrophe.

Postmitotic cells that are treated with TTFIELDS and aberrantly exit mitosis develop aneuploidy, and these aneuploid cells are in general resistant to apoptosis, a process that is known to trigger an immunosuppressive response in the host.^{13,14} However, TTFIELDS also cause cytoplasmic stress and additional signs of immunogenic cell death, including high mobility group box 1 (HMGB1) secretion into the extracellular space, calreticulin upregulation on the cell surface, and annexin V binding.^{15,16} These findings suggest that TTFIELDS may increase the immunogenicity of tumor cells *in vivo*. When highly metastatic VX-2 tumors were injected into the kidney capsules of rabbits and were treated with TTFIELDS for 7 days after their establishment, metastases to the lungs were markedly reduced compared with non-treated animals. Recovered lung metastases also revealed a significant increase in infiltration of immune cells within the tumors.^{17,18} An interpretation of these results is that TTFIELDS acted to sensitize the animals against metastatic spread and that the increased leukocytic infiltrates reflected an increased requirement for the immunosuppressive stroma for their establishment and maintenance. As discussed later, patients treated with the immunosuppressive steroidal anti-inflammatory drug dexamethasone seem not to respond to TTFIELD treatments and those with higher levels of CD3⁺, CD4⁺, and CD8⁺ lymphocytes are more likely to have a better outcome on this therapy.¹⁹ Collectively, these data strongly support an immunologic basis for the antitumor response from TTFIELD treatment.

Physical Properties of Tumor-treating Fields and Electric Field Distribution Within the Brain

The physical effects of TTFIELDS are governed by the fundamental physics of Gauss' law, Ohm's law, the continuity equation, and Coulomb's law.²⁰ In addition, several factors, including a medium's electrical conductivity (a measure of the ability to pass charges) and relative permittivity (a measure of the ability to hold charges), can affect the electric field distribution within the brain tissue. Because each tissue type is unique, the intracranial structures must therefore be characterized based on their conductivity and permittivity values. The highly heterogeneous

consistency and geometry of the brain therefore distort the intracranial electric fields as induced by an external source. Electric fields are generally defined by instantaneous changes in electric potential. These changes in electric potential result in electromotive disruption of mitotic structures and are therefore the basis for the therapeutic benefit of TTFIELDS.^{9,10} TTFIELD therapy for glioblastoma is delivered by 2 pairs of transducer arrays positioned orthogonally on the shaved scalp, adhered by a thin layer of conductive gel that provides good conductivity (Fig. 17.3).^{20,21} TTFIELDS are generated by a battery-powered alternating current generator, operating at 200 kHz with maximum voltage alternating from +50 to -50 V.

To obtain a comprehensive model of the electric field's distribution in the brain, computer modeling can be performed using coregistered patient DICOM (Digital Imaging and Communications in Medicine) data sets from T1-weighted postgadolinium, T2, and MPRAGE (Magnetization-Prepared Rapid Acquisition with Gradient Echo) MRI. Previously, Lok and colleagues²² showed a heterogeneous distribution of electric fields in the brain, and the regions adjacent to the ventricular horns had a particularly high electric field intensity (Fig. 17.4). This high field intensity is likely caused by the higher electric conductivity of cerebrospinal fluid than the surrounding tissues, which behaves like the terminal of a capacitor, with the surrounding tissues functioning like a dielectric between conductive terminals. Since a dielectric medium generally retains charge, the rate at which the medium is able to collect and retain the charge is defined by its conductivity and relative permittivity. At 200 kHz, the effect of permittivity is overwhelmed by the conductivity of the medium (Fig. 17.5).²³ Furthermore, each medium has a unique capacitive reactance characteristic of the medium's conductivity, and the rate at which the medium is able to collect and retain charges is frequency dependent. At high frequencies, the medium only has limited time to collect a finite amount of charges and retain them before the field collapses as the polarity changes direction, thereby discharging the initially retained charges before repeating the process.

Because cerebrospinal fluid has a low permittivity value compared with its surrounding tissues, it is a poor dielectric medium and thus charges migrate through the fluid layer at a much faster rate with minimal charge retention. This property explains why most of the cerebrospinal fluid has very low electric field intensity. But this is not true at the interface between cerebrospinal fluid and its adjacent brain tissue. For a perfect solid

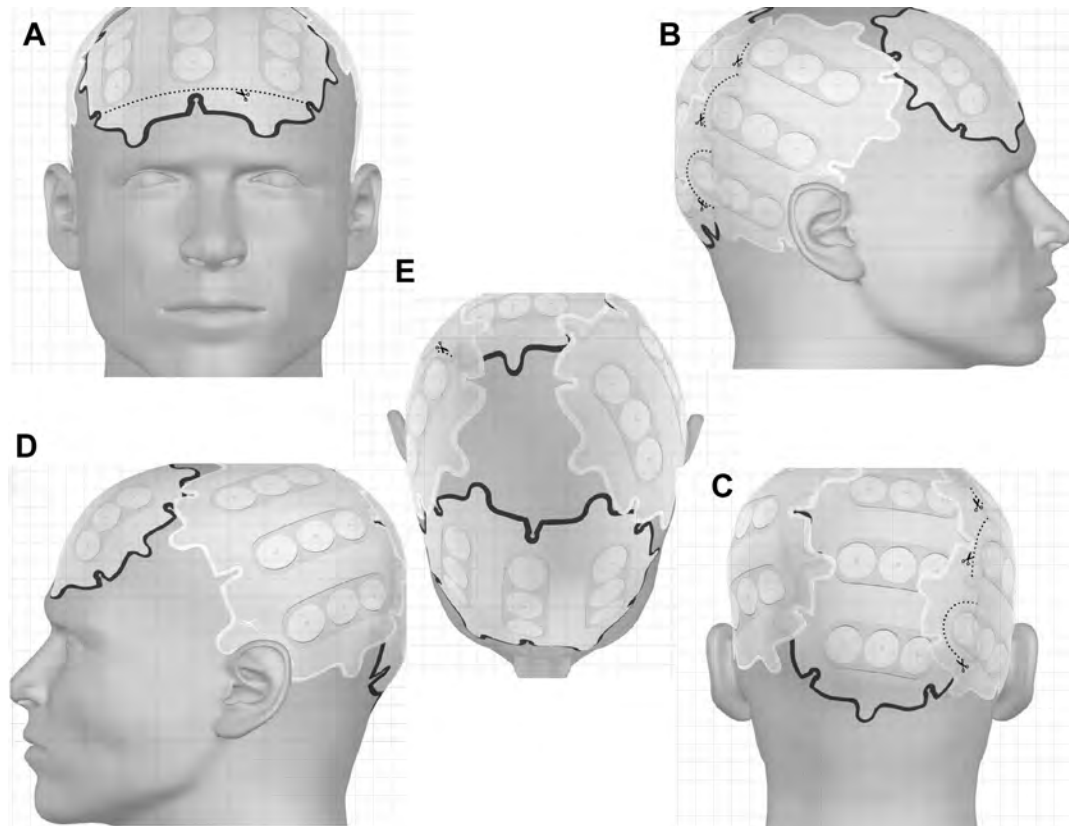


Fig. 17.3 Transducer array placement for TTFields therapy. TTFields are delivered by 2 pairs of transducer arrays placed orthogonally (A–E) on the shaved scalp. The arrays are connected to a battery-operated current generator, operating at 200 kHz with peak-to-peak voltage from +50 to –50 V.

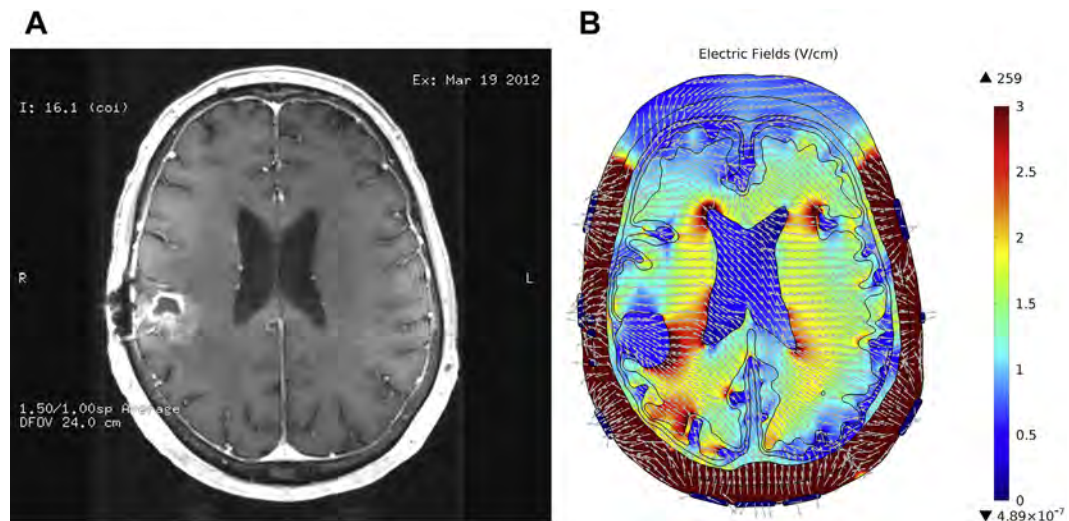


Fig. 17.4 Intracranial distribution of TTFields. Computed modeling of a patient’s recurrent glioblastoma in the right parietal brain (A) revealed inhomogeneous electric field distribution within the intracranial space (B). High field strength was seen at the ventricular horns and the medial aspect of the tumor facing the lateral ventricle.

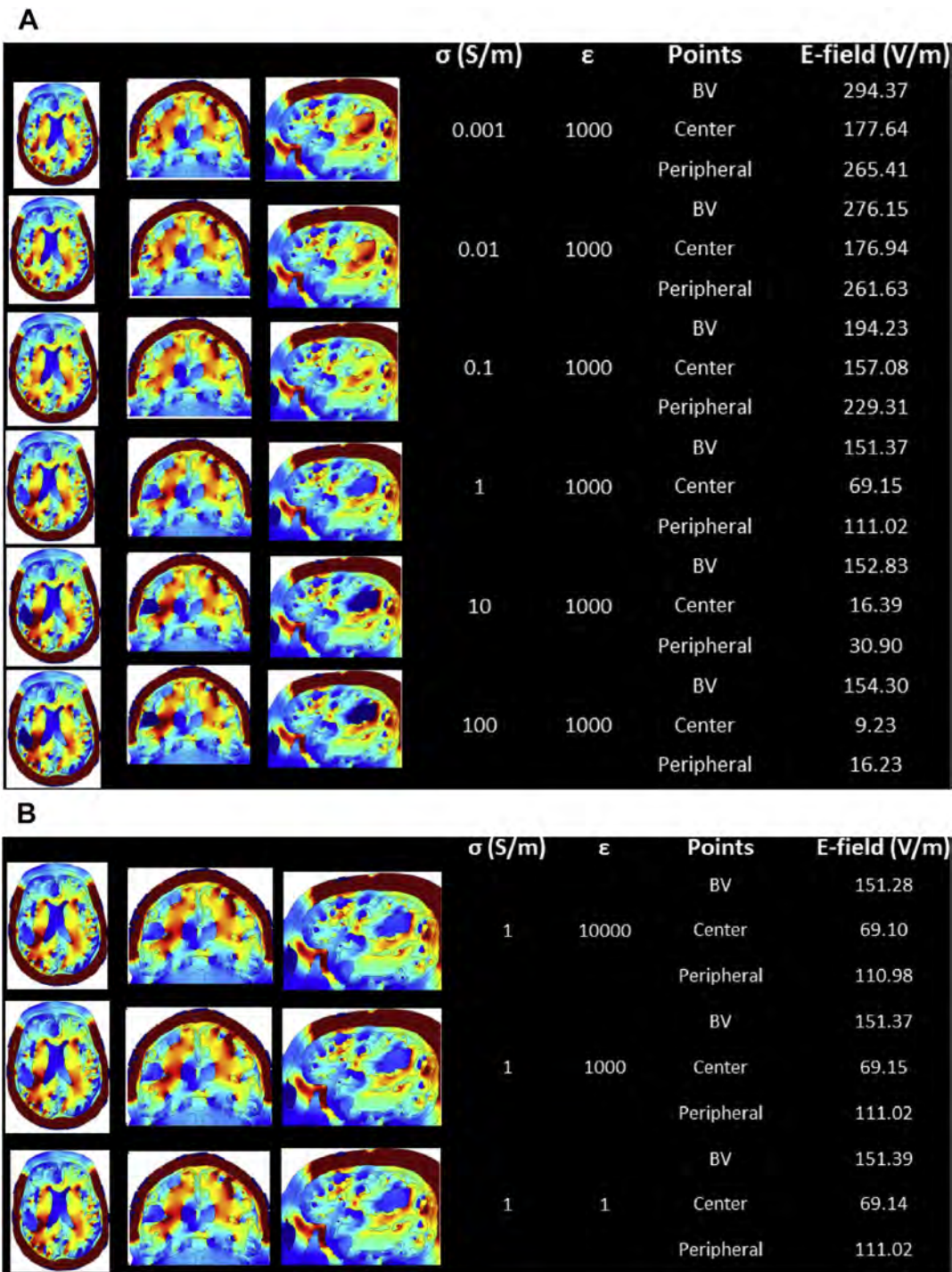


Fig. 17.5 Sensitivity analysis of the electric field distribution in the gross tumor volume (GTV) as a function of conductivity or permittivity. (A) The electric field intensity of the GTV and the surrounding tissues decreased as the conductivity increased from 0.001 to 100 S/m. (B) However, the electric field intensity and distribution did not change significantly as permittivity varied from 1 to 10,000. BV, bilateral ventricles.

conductor, the electric field within it is zero, and the charges are uniformly distributed on the surface of the conductor. However, cerebrospinal fluid is neither a perfect conductor nor a dielectric.

When charges are positioned across a parallel flat surface, repulsive forces are generated and the charges dissipate away from each other. However, on surfaces with very steep geometric gradients

(ie, sharp corners), the repulsive forces are greatly increased because the charge density is much higher within a smaller surface area. Therefore, it is expected that the ventricular horns have a significantly higher electric field intensity than the rest of the cerebrospinal fluid space as a result of the bunching effect of charge distribution in a region with an irregularly sharp geometry.

The electric properties of gliomas can also vary among patients depending on their tumor composition. Tumors with larger necrotic cores are likely to have higher field intensities in the gross tumor volume because of the capacitive reactance, as explained earlier. In contrast, tumors with smaller or no necrotic core are likely to have lower field intensities at the center of the volume because of absence of an adjacent conductive medium to act as an electric current source. This property may become clinically relevant due to the increased requirement for time of exposure to TTFields as the outer layers of the gross tumor volume are treated by lower field intensities.

EVIDENCE FOR THE USE OF TUMOR-TREATING ELECTRIC FIELDS IN THE TREATMENT OF RECURRENT AND DE NOVO GLIOBLASTOMAS

First-in-Human Tumor-Treating Fields Therapy for Glioblastoma

The first-in-human pilot trial for safety and efficacy of TTFields therapy was conducted in Europe from 2004 to 2005 and enrolled 10 patients with recurrent glioblastoma.⁸ The most common adverse event was contact dermatitis, which occurred in 9 patients and was thought to be a result of hydrogel-induced irritation on the scalp. Two patients experienced partial seizures that were related to their tumors. No toxicity on blood count or chemistry was seen, except for increased liver enzyme levels in those taking anticonvulsants. The median overall survival (mOS) of the 10 patients was 14.4 months. The time to tumor progression was 6.0 months and the 1-year overall survival (OS) rate was 67.5%, which compared favorably with the historical data of 5.8 months for mOS, 2.1 months for median progression-free survival (mPFS), and 21% for 1-year OS.^{8,24} There was 1 complete and 1 partial responder who were alive at 84 and 87 months, respectively, from treatment initiation.²⁵ Importantly, the intensity of electric fields as directly measured in 1 patient was validated to be within 10% of the values estimated by computer modeling of the electric field distribution within the brain.⁸

A concurrent pilot study was conducted from 2005 to 2007 that enrolled 10 patients with newly

diagnosed glioblastoma.²⁵ TTFields were added to adjuvant temozolomide after initial standard-of-care radiotherapy and concomitant daily temozolomide.²⁶ The mPFS was 35.8 months and mOS was greater than 39 months, which compared favorably with the mPFS of 6.9 months and mOS of 14.6 months from the data in the phase III trial.^{25,26} The only adverse event noted in the pilot cohort was scalp dermatitis, and that could be ameliorated by topical corticosteroids and periodic shifting of transducer arrays.²⁵ There were 2 long-term survivors who lived 84 and 64 months from their initial diagnoses.²⁵

Tumor-Treating Fields for Recurrent Glioblastoma

The phase III pivotal trial of TTFields for recurrent glioblastoma was conducted from 2006 to 2009 and the primary end point was OS (NCT00379470).²⁷ In the intent-to-treat population, the median OS was 6.6 months for subjects treated with TTFields versus 6.0 months for those who received best physician's choice (BPC) chemotherapy, with a hazard ratio of 0.86 ($P = .27$) (Fig. 17.6). About 31% of the BPC chemotherapy cohort received bevacizumab alone or in combination with chemotherapy. The mPFS was 2.2 and 2.1 months respectively for TTFields and BPC chemotherapy treatment, with a hazard ratio of 0.81 ($P = .16$). The progression-free survival (PFS) at 6 months was 21.4% and 15.1%, respectively ($P = .13$). The 1-year survival rate was 20% in both cohorts. The outcome of the trial indicated that TTFields probably had efficacy comparable to chemotherapy and bevacizumab.

Grade 1 or 2 scalp irritations were the most common adverse events associated with the device. Shifting the arrays slightly during array exchange and applying topical corticosteroid can minimize this irritation.²⁸ There were far less hematological toxicity, appetite loss, constipation, diarrhea, fatigue, nausea, vomiting, and pain associated with the device when compared to BPC chemotherapy. Furthermore, analysis showed that device-treated patients had better cognitive and emotional functions. Based on the comparable efficacy results and absence of serious TTField-associated toxicities, the US Food and Drug Administration (FDA) approved TTFields therapy on April 8, 2011 for the treatment of recurrent glioblastoma.

The discrepancy in the OS rates between the results of the phase III trial and the robust outcome from the first-in-human pilot study prompted a series of *post hoc* analyses of the trial data. The first analysis centered on responders. This analysis showed that 5 of 14 responders treated with

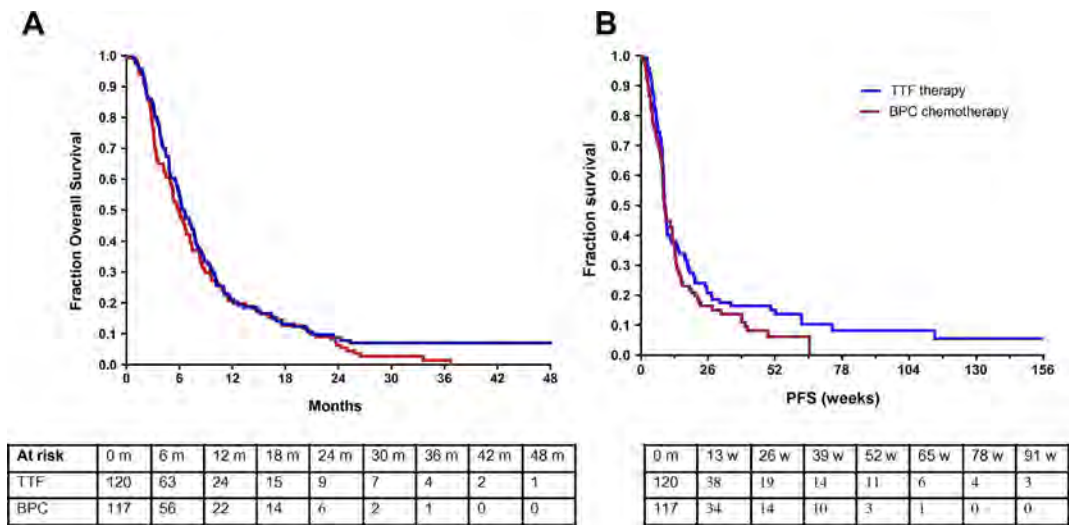


Fig. 17.6 Intent-to-treat Kaplan-Meier OS and PFS curves in the pivotal trial for patients with recurrent glioblastoma comparing TTField therapy with BPC chemotherapy. (A) The median OS was 6.6 months for patients treated with TTFields versus 6.0 months for those received BPC chemotherapy, with a hazard ratio of 0.86 ($P = .27$). (B) The median PFS was 2.2 and 2.1 months respectively for TTFields and BPC chemotherapy treatment, with a hazard ratio of 0.81 ($P = .16$). TTF, TTFields.

TTField monotherapy had prior low-grade histology, whereas none of the 7 responders treated with BPC chemotherapy did.²⁹ Second, the analysis revealed significantly less dexamethasone use in responders when compared to nonresponders.²⁹ Responders in the TTField monotherapy group received a median dexamethasone dose of 1.0 mg/d while nonresponders received 5.2 mg/d. A similar difference was also noted in the median cumulative dexamethasone dose of 7.1 mg for responders compared to 261.7 mg for nonresponders. In the chemotherapy cohort, the median dexamethasone dose used was 1.2 mg/d for responders while it was 6.0 mg/d for nonresponders. However, the median cumulative dexamethasone dose was not significantly different: 348.5 mg for responders versus 242.3 mg for nonresponders. These data suggest that TTFields efficacy may be influenced by concurrent dexamethasone use, which is a clinically modifiable factor. This finding prompted an in-depth analysis of the dexamethasone effect in the entire trial population.

Applying an unsupervised modified binary search algorithm that stratified the TTField monotherapy arm of the phase III trial based on the dexamethasone dosage that provided the greatest statistical difference in survival revealed that subjects who used greater than 4.1 mg/d of dexamethasone had a markedly shortened median OS of 4.8 months compared with those who received less than or equal to 4.1 mg/d, who had a median OS of 11.0 months (Fig. 17.7).¹⁹ Subjects in the chemotherapy arm were observed to have a

similar, but less robust, dichotomization and those who used greater than 4.1 mg/d and less than or equal to 4.1 mg/d of dexamethasone had a median OS of 6.0 and 8.9 months, respectively. This difference in OS based on dexamethasone dose was unrelated to tumor size but was most likely caused by interference with patient immune effector function. A single-institution validation cohort of patients treated with TTField therapy, using their CD3⁺, CD4⁺, and CD8⁺ T lymphocyte levels as a marker of immune competency, suggested the importance of immune competence to TTField therapy. Importantly, a dexamethasone dosage of greater than 4.0 mg/d was also a poor prognostic factor in newly diagnosed patients who completed radiotherapy,³⁰ supporting the conclusion that dexamethasone can interfere with treatment. With successive increases in dexamethasone dosage, both cohorts reached an inflection point near 8.0 mg/d, after which the rate of survival decreased slowly. Taken together, dexamethasone exerts a generalized and profound interference on the efficacy of both TTFields and chemotherapeutic treatment against glioblastoma. Therefore, dexamethasone use should be aggressively minimized.^{19,31}

Use of Tumor-Treating Fields Therapy in Clinical Practice

The post-FDA-approval usage of TTField therapy in routine clinical practice may differ from that in the registration trial, primarily because clinical trial data may not always be representative of

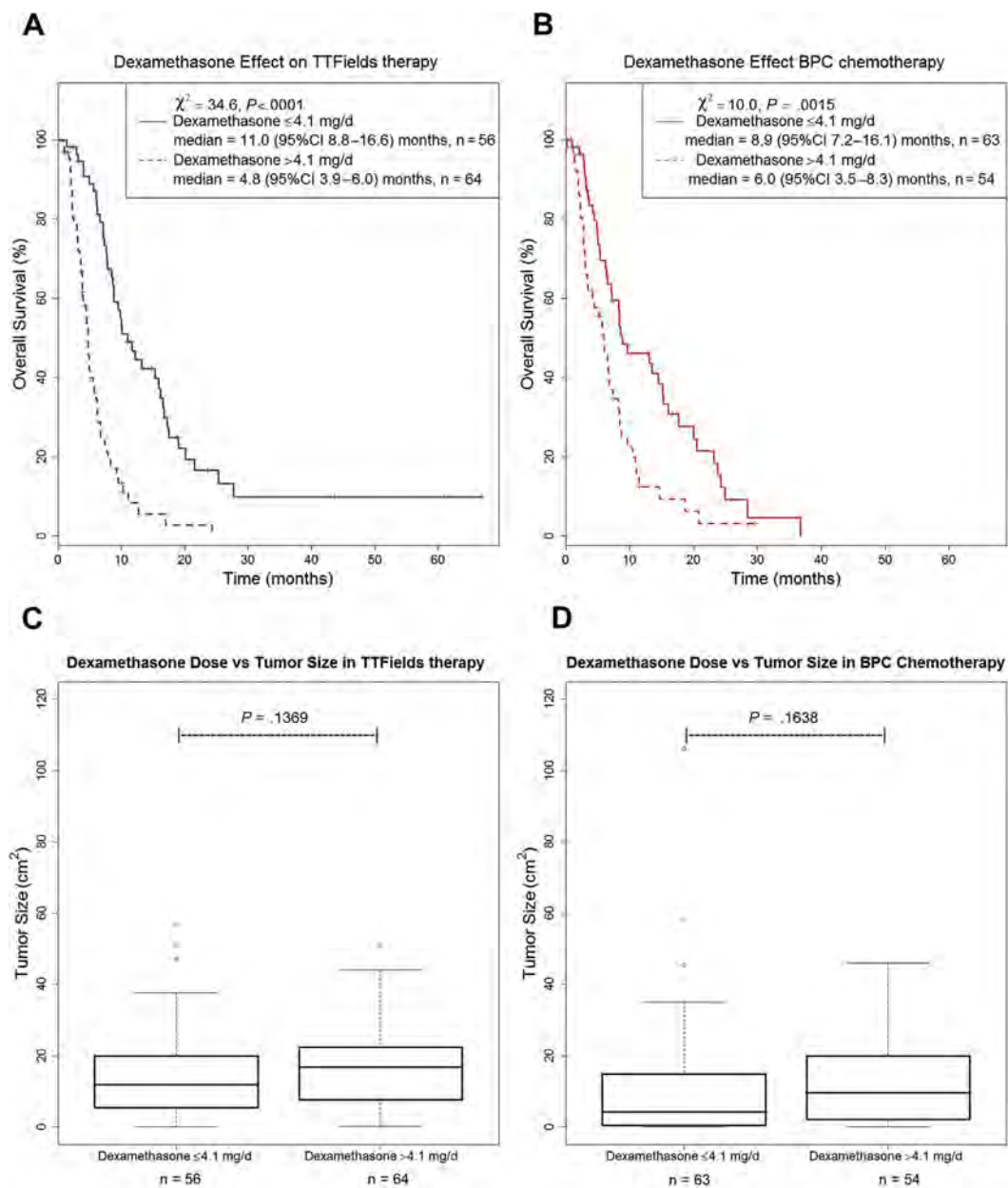


Fig. 17.7 Kaplan-Meier OS and tumor size with respect to dexamethasone requirement of less than or equal to 4.1 mg/d versus greater than 4.1 mg/d from subjects enrolled in the phase III trial comparing TTField therapy with BPC chemotherapy. (A) Subjects enrolled in the TTField treatment arm taking dexamethasone less than or equal to 4.1 mg/d (solid blue) versus greater than 4.1 mg/d (dashed blue), which was determined by an unsupervised binary partitioning algorithm. Subjects who used less than or equal to 4.1 mg/d of dexamethasone (n = 56) had a median OS of 11.0 months (95% confidence interval [CI], 8.8–16.6) compared with those who used greater than 4.1 mg/d (n = 64), who had a median OS of 4.8 months (95% CI, 3.9–6.0) ($\chi^2 = 34.6$; $P < .0001$). (B) Subjects enrolled in the BPC chemotherapy arm taking dexamethasone less than or equal to 4.1 mg/d (solid red) versus greater than 4.1 mg/d (dashed red), which was determined by the same unsupervised binary partitioning algorithm. Subjects who used less than or equal to 4.1 mg/d of dexamethasone (n = 63) had a median OS of 8.9 months (95% CI, 7.2–16.1) compared with those who used greater than 4.1 mg/d (n = 54), who had a median OS of 6.0 months (95% CI, 3.5–8.3; $\chi^2 = 10.0$; $P = .0015$). (C) Box-and-whisker plot of bidimensional tumor size in the TTField therapy cohort that received dexamethasone less than or equal to 4.1 mg/d versus greater than 4.1 mg/d. Subjects who took dexamethasone less than or equal to 4.1 mg/d (n = 56) had a median tumor size of 11.9 cm² (range, 0.0–56.7 cm²) compared with those who used greater than 4.1 mg/d (n = 64), who had a

treatment outcome in routine clinical practice environments. Reasons for this discrepancy may arise from the prespecified clinical characteristics that trial subjects must possess that real-world patients may not have. As a result, trial subjects typically have healthier neurologic functions, better performance status, and fewer medical comorbidities, all of which may enable trial subjects to benefit more from the new treatment. Furthermore, the FDA must strike a fine balance between providing the public rapid access to new treatments for deadly diseases and requiring comprehensive data and protracted reviews on their benefits and risks. This action sometimes results in the reversal of prior accelerated approval decisions. Therefore, these issues prompted the development of the Patient Registry Data Set (PRiDe) to capture data on TTField usage among patients in the routine clinical practice environment.

PRiDe consisted of 457 patients from 91 treatment centers in the United States. Patients treated in PRiDe had a median OS of 9.6 months compared with 6.6 months in the TTField monotherapy arm in the registration trial.^{27,32} The 1-year OS rate was also longer at 44% compared with 20%, respectively.^{27,32} The difference in survival characteristics is most likely caused by the higher proportion of patients treated with TTFields at first recurrence in PRiDe (33%) than in the registration trial (9%). Treatment at an earlier timepoint in the disease process may provide a higher efficacy than treatment at a later timepoint. Absence of prior bevacizumab usage was also favorable.³² Nevertheless, the heterogeneity in the adjunctive treatments used in conjunction with TTField therapy in PRiDe that was not adequately captured, which included cytotoxic chemotherapy, bevacizumab, or even alternative medicine, is an important caveat that makes it statistically noncomparative with the TTField monotherapy arm in the phase III trial.

Efficacy of Tumor-Treating Fields Therapy for Newly Diagnosed Glioblastoma

A phase III randomized open-label study of TTField therapy was conducted in 700 patients with newly diagnosed glioblastoma between 2009 and 2014 (NCT00916409). After their initial

radiotherapy and concomitant daily temozolomide, subjects were randomized in a 2:1 fashion to receive either TTFields plus maintenance temozolomide or maintenance temozolomide alone.³³ The primary end point was PFS. In a prespecified interim analysis of the first 315 subjects after a minimum follow-up of 18 months, the intent-to-treat cohort that received TTFields plus temozolomide had a longer PFS than the cohort treated with temozolomide alone: median 7.1 versus 4.0 months (hazard ratio = 0.62; 95% confidence interval [CI], 0.43–0.89; log rank P = .0014) (Fig. 17.8). The median OS also favors the TTFields plus temozolomide group, at 19.6 versus 16.6 months respectively (hazard ratio = 0.74; 95% CI, 0.56–0.98; log rank P = .034), as well as the per protocol population that completed more than 1 cycle of treatment, at 20.5 versus 15.6 months respectively (hazard ratio = 0.64; 95% CI, 0.42–0.98; log rank P = .004).

The trial population experienced no unexpected adverse events.³³ Grade 3 and 4 hematological toxicities between the TTFields plus temozolomide and temozolomide alone cohorts (12% vs 9%), gastrointestinal disorders (5% vs 2%), and convulsions (7% vs 7%) were not significantly different. Only scalp reaction was more commonly seen in those who received TTFields plus temozolomide. Based on the favorable efficacy and toxicity data, the US FDA granted approval on October 5, 2015 to use TTFields in conjunction with maintenance temozolomide in the adjuvant setting for patients with newly diagnosed glioblastoma.

SUMMARY

Human clinical trial testing of TTField efficacy was started in neuro-oncology, initially for the treatment of recurrent glioblastoma (NCT00379470) and later in newly diagnosed glioblastoma (NCT00916409).^{27,33} This route of development for a new anticancer therapy is highly unusual because treatments in neuro-oncology were traditionally adopted from established therapies from other disease sites, when the accompanying preclinical scientific data on the mechanisms of action had been firmly established. Nevertheless, the 2 pivotal trials conducted in glioblastoma have

median tumor size of 16.8 cm² (range, 0.3–51.0 cm²). (P = .1369). (D) Box-and-whisker plot of bidimensional tumor size in the BPC chemotherapy cohort that received dexamethasone less than or equal to 4.1 mg/d versus greater than 4.1 mg/d. Subjects who took dexamethasone less than or equal to 4.1 mg/d (n = 63) had a median tumor size of 4.2 cm² (range, 0.0–11.2 cm²) compared with those who used greater than 4.1 mg/d (n = 54), who had a median tumor size of 9.6 cm² (range, 0.0–46.0 cm²) (P = .1638).

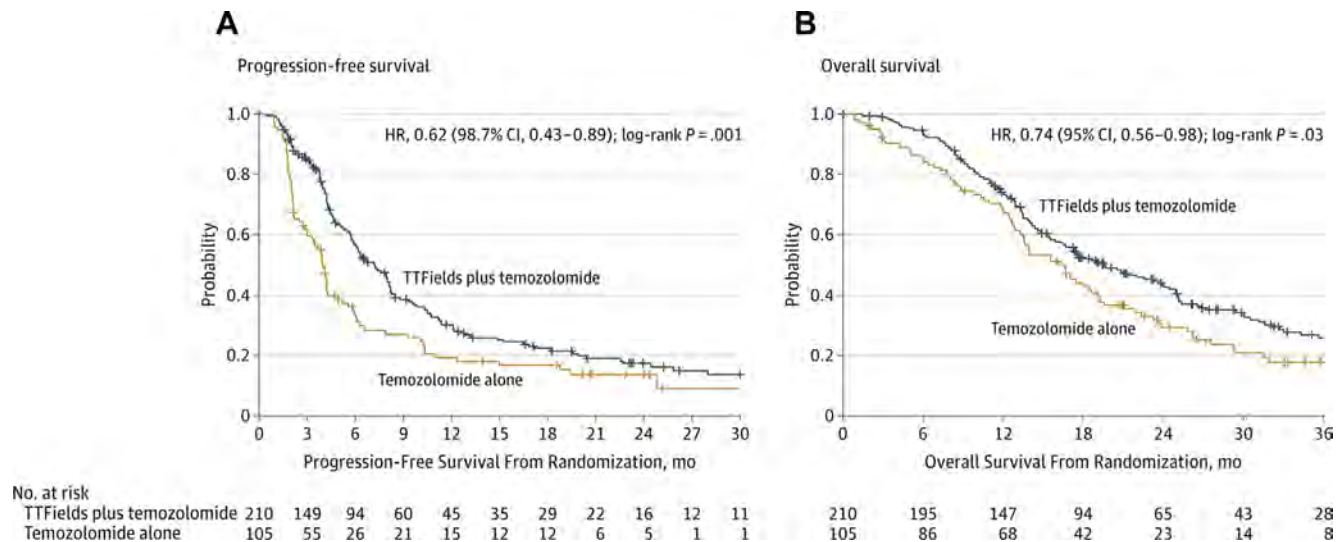


Fig. 17.8 Prespecified interim analysis of PFS and OS in registration trial for patients with newly diagnosed glioblastoma comparing maintenance TTFields therapy plus temozolomide versus temozolomide alone. Kaplan-Meier comparison of the two cohorts showed (A) a median PFS of 7.1 versus 4.0 months respectively, with a hazard ratio of 0.62 ($P = .0014$), and (B) a median OS of 19.6 versus 16.6 months respectively, with a hazard ratio of 0.74 ($P = .034$).

helped to established TTFields as a *bona fide* anti-cancer treatment and its efficacy is being actively investigated in glioblastoma as well as other malignancies both within and outside the central nervous system.

To improve the efficacy of TTFields treatment of recurrent glioblastomas, there is a strong rationale for combining it with SRS. Large-fraction radiotherapy might potentiate immune-mediated antitumor activity.^{34,35} The addition of TTFields after SRS may further potentiate this effect because exposed tumor cells show cell surface expression of calreticulin and secretion of HMGB1, both of which are required to generate immunogenic cell death.^{15,36,37} Furthermore, a *post hoc* analysis of the phase III trial for recurrent glioblastoma showed that the application of TTFields among subjects who had progressed on bevacizumab ($n = 23$) resulted in a longer mOS of 6.0 months compared with a mOS of 3.3 months ($n = 21$) in those treated with BPC chemotherapy (hazard ratio = 0.43; 95% CI, 0.22–0.85; $\chi^2 P = .06$).³⁸ In addition, the favorable intracranial safety profile of TTFields and bevacizumab suggests that the combination will most likely have an acceptable level of toxicity.^{38,39} There is a planned Radiation Therapy Oncology Group foundation study on TTFields and bevacizumab in patients with recurrent glioblastoma who have progressed while on bevacizumab.

Several investigator-initiated combination trials are being conducted using (1) TTFields in combination with bevacizumab and carmustine in patients with glioblastoma at first relapse (NCT02348255), (2) TTFields with bevacizumab and hypofractionated stereotactic radiotherapy for bevacizumab-naïve patients with recurrent glioblastoma (NCT01925573), and (3) TTFields in combination with temozolomide and bevacizumab for patients with newly diagnosed glioblastoma in the maintenance phase of treatment, after initial radiotherapy with concomitant temozolomide and bevacizumab (NCT02343549). In addition, a study has been designed to find genomic signatures of recurrent glioblastoma that may correlate with response to TTFields (NCT0194576). Collectively, these planned and ongoing studies indicate the current state of interest in combining TTFields with other established modalities of treatment for glioblastoma.

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Alternating Electric Fields Therapy in Oncology

A Practical Guide to
Clinical Applications of
Tumor Treating Fields

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Editor



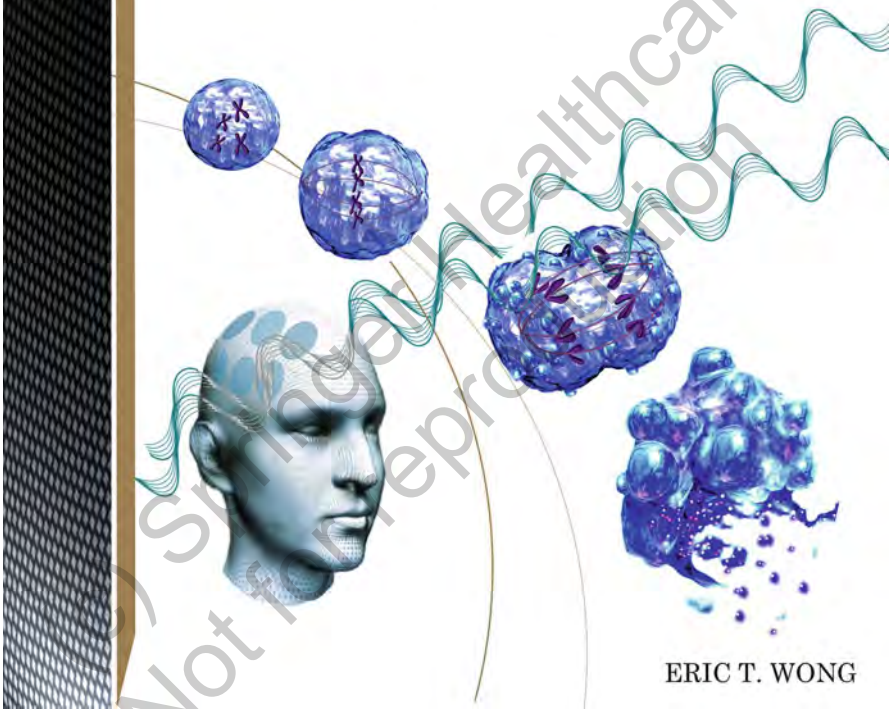
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ALTERNATING ELECTRIC FIELDS THERAPY IN ONCOLOGY

A PRACTICAL GUIDE TO CLINICAL
APPLICATIONS OF
TUMOR TREATING FIELDS



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of Tumor Treating Fields



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Preface

“Questioning our own beliefs in this way (...challenging our assumptions...) isn’t easy, but it is the first step in forming new, hopefully more accurate, beliefs.”

Duncan J. Watts in *Everything is Obvious*

When Mike Ambrogi from Novocure sat down in my office for the first time in 2006 showing me a time-lapse video, I was mesmerized by the cells “blowing up” under the influence of alternating electric fields or Tumor Treating Fields. At that time, he was trying to enlist sites to participate in Novocure’s EF-11 phase III clinical trial comparing a device that emits these fields to chemotherapy for recurrent glioblastoma. The device was strange because it required shaving of the patient’s head and applying to the scalp four transducer arrays and each one had a set of nine ceramic disks. There were wires connecting the arrays to a box that generated the electric fields. At that time, *The Matrix* and its sequels were topping the box office and permeating popular culture. I was wondering whether or not this was the beginning of a brain-machine interface for the treatment of brain cancer. But in all seriousness, two killer questions came to my mind after seeing the video that led to our research team’s long-term commitment in this scientific exploration: (1) Did the alternating electric fields at 200 kHz (10^3 Hz) permeate from the surface of the scalp into the brain, and (2) what was the biological mechanism causing the cells to blow up? The answer to the first question was easier to find. This took me back to my undergraduate senior design project at UPenn’s engineering school when I was working on optimizing electronic circuits in the gigahertz (10^9 Hz) range or the microwave part of the electromagnetic spectrum. One thing I learned from the experience was that whether or not an alternating signal bounces from or penetrates into an object really depends on its frequency. Fortunately, a paper published in 1996 had a “spec sheet” on the dielectric properties of skull, gray matter, and white matter in the kilohertz range. It showed that the permittivity (the ability to hold charges) and conductivity (the ability to pass charges) of the three structures are similar and all of parameters are within an order of magnitude from each other, suggesting that the electric fields

at 200 kHz can permeate skull, gray matter, and white matter as if they were one continuous medium. This is similar to light passing through a window into your living room—you are able to read a book either inside or outside of your home.

The second question was harder to address because there was still a lot of uncertainty in the cell biology effects from the electric fields at 200 kHz. I took the video on Tumor Treating Fields to Lew Cantley's lab in the Division of Signal Transduction and showed it to multiple postdoctoral researchers there. There were a lot of comments like "cool," "interesting," "far out" ... etc. Ken Swanson was one of them but, like me, he was also mesmerized by the video. He reviewed the video multiple times over a few days, like a child watching cartoons over and over as if each time was a new experience. He made one very important observation and pointed out that after the cells underwent violent blebbing, they spread out and went back into the tissue culture—they did not die or dissociate from the dish. We both concluded that more cell biology experiments needed to be done and, after obtaining an unrestricted sponsored research agreement, we discovered that the blebbing process is a result of disrupted septins causing disorganized cytokinesis when cells transition from metaphase to anaphase. The aftermath of this disruption is aberrant mitotic exit, asymmetric chromosome segregation, and eventually immunogenic cell death. At about the same time, the results of the EF-11 trials came out and the device was approved by the U.S. Food and Drug Administration in 2011 for use in patients with recurrent glioblastoma and, later in 2015, for newly diagnosed glioblastoma.

Ed Lok is the third member of our research team, and he is the driving force behind our understanding of the electric field distributions in the brain. He has degrees in physics from college and radiation physics from graduate school, and he now works as a full-time medical physicist. He is intensely interested in the application of medical physics in medicine and after 8 years on our team he is still determined to figure out the most accurate method for delineating these tumor treating electric fields in the brain.

I learned an invaluable lesson while performing this translational research. I realized how different the training of a physician is from that of a research scientist, regardless of the subject of investigation such as addressing unanswered questions in basic biological sciences or testing the efficacy of new medical treatments. A clinician's job is to properly diagnose and appropriately treat a patient's ailment, and this is done by taking a careful history and observing the patient, as well as using whatever diagnostic tests that are available to arrive at a set of diagnoses that best fit the available data. Through a process of elimination, which is a weighted assessment based on the clinical acumen of that physician or the results from additional diagnostic tests, the clinician will then arrive at a "best fit" diagnosis and then treat the disease accordingly. In contrast, an investigator's job is find answers to an unexplained observation or question. It is dangerous to go into a scientific investigation with a preconceived notion of outcome. Quite often, these preconceived ideas reside in our subconscious and they can wholeheartedly interfere with the proper interpretation of observations and empirical data, particularly when conflicting

results are present. In my experience, a seasoned scientist or investigator is more receptive to outlandish ideas than clinicians, probably because the latter are conditioned in a Pavlovian fashion to find the “best fit” explanation. Therefore, as commented in Duncan Watts’ book, *Everything is Obvious*, questioning my own beliefs is essential in forming new, and hopefully more accurate, beliefs.

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Acknowledgements

This is the first textbook on alternating electric fields in oncology—also known as Tumor Treating Fields—and I certainly could not have accomplished this work without the help of others. I thank my longtime collaborators, Ken Swanson and Ed Lok, for working with me on this subject for nearly a decade, as well as Novocure for providing an unrestricted sponsored research agreement so that we can address some of the fundamental questions on Tumor Treating Fields in our laboratory. I am also indebted to contributors of this book who found the time and energy to write chapters that are essential for current understanding of this anti-cancer treatment. My neurology chief of service at Beth Israel Deaconess Medical Center Clif Saper is equally supportive of my clinical and research endeavors. Although protected time is often a sought after commodity in academic medicine, changes in the health care environment and federal funding structure in the United States make it increasingly challenging. But I am fortunate to have extraordinary support at work and at home. Deborah Cooper, Julianne Bloom, and Loretta Barron are the staff members in the brain tumor clinic who have been working with me for over a decade and they are instrumental in helping me care for a large number of complex patients. Lastly, my wife Ling and my daughter Erika are the two individuals at home who make my after-work moments enjoyable, not to mention my wife's green chiffon cake and her gourmet Trung Nguyễn Vietnamese coffee that really improve my ability to do academic work. Likewise, I totally enjoy being a coach in Erika's Math League program in elementary school, where I have an opportunity to explain abstract concepts to her and her friends while simultaneously watching them learn.

There are a number of other individuals who helped me tremendously in compiling this book. Those who made this work possible include Greg Sutorius and Mariah Gumpert from Springer who helped with the publishing process, Janlyn Murphy who proofread a number of chapters, and Barbara Beiss from Novocure who helped me to get permission for a number of copyrighted figures from various publishers.

Kisa Zhang was instrumental in creating the beautiful digital artwork, and she was especially good at translating concepts in physics and biology into visual art. Finally, my patient Tom DesFosses, a brain tumor survivor, and his wife Judy DesFosses are two individuals who provided me unwavering support for nearly a decade with their optimism and their fundraising efforts in *A Reason to Ride* annual bikeathon.

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Chapter 1

Cell Biological Effects of Tumor Treating Fields

Nidhi Gera and Kenneth D. Swanson

Application of Electric Fields to Patient Care

Electrotherapy involves the use of electrical energy for the treatment of medical conditions. Starting in the mid to late 1800s there was a fascination with the possible effects of electricity on the human body. This led to a proliferation of electricity-based devices that claimed to treat various maladies. While there were a limited number of cases where these devices led to the development of standard medical equipment, such as physiotherapeutic devices used to prevent muscle atrophy and cardiac defibrillators developed to stop arrhythmia, most early attempts proved to have little efficacy beyond possible placebo effects [1].

The biologic effects of electric fields within different tissues are dependent on both the intensity and frequency of the stimulating electric field or current. Different frequencies have vastly different biologic effects. For instance, at 1 kHz or lower, alternating electric fields cause depolarization of membrane potentials in excitable cells, such as neurons, cardiac myocytes, and muscle cells, via opening of voltage-gated ion channels [2–4]. Defibrillators, electro-shock therapy, and neuromuscular stimulation of muscles all rely on their ability of high intensity electric fields to induce membrane depolarization. In an early attempt to test whether electric fields were able to directly affect cellular physiology at a more molecular level, Rosenberg et al. [5] in 1965 at Michigan State University exposed *E. coli* cultures to electric fields generated by immersing platinum electrodes into the broth. This led to a

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reduction in cell division, but not cell growth, resulting in the elongated growth of the bacteria [5]. This suggested that their cell division was sensitive to perturbation by electric fields. However, it was subsequently demonstrated that the media contained cisplatin produced *de novo* upon passing electric current through the platinum electrodes during the course of the experiment. This was found to be responsible for the observed growth effects [6]. Fortuitously, while this attempt failed to demonstrate the effects of electric fields on cellular function, it was later found that cisplatin, produced by the electrodes during this experiment, had potent anti-mitotic effects on cancer cells and is now a commonly used cancer chemotherapeutic [7].

Tumor Treating Fields

Dr. Yorum Palti, emeritus professor at the Rappaport Institute in Israel, developed a technology to deliver electric fields to tumor cells without such chemical alterations to the media by using insulated electrodes. In these experiments, cell viability was profoundly affected at frequencies between 100 and 250 kHz. More precise measurements of cell viability revealed a reasonably tight peak of this cytotoxic effect in all cell types tested between 150 and 200 kHz, with little or no effect being detectable at frequencies below 50 kHz or above 500 kHz. The effect of these alternating electric fields also increased with field intensity. Given their cytotoxic effects these alternate electric fields within this frequency range were referred to as Tumor Treating Fields (TTFields) [8, 9]. Cells exposure to TTFields within mitosis exhibited violent membrane blebbing [9] and exposed cells have also been shown to be increased in volume [10]. While possible, no other clearly defined effects on cellular physiology have yet been reported for TTFields. When treated cell cultures were stained for tubulin and DNA it was found that spindle elements and the mitotic chromosomal order were disrupted. One of the more enigmatic features of TTFields' biophysical impact on cells is that the incident angle to the mitotic plate dictates the magnitude of cellular damage. When the TTFields were aligned perpendicular to the plane of division, cells were relatively unaffected, whereas cells exhibited a higher degree of mitotic failure if the TTFields were oriented parallel to the plane of division [9].

TTFields-induced mitotic disruption occurs coincident with cells exit from metaphase. Early reports showed that cells exposed to TTFields exhibited increased time in mitosis [9, 11]. Our laboratory showed that there was no gross perturbation in transit that would suggest a block during metaphase exit [12]. We found that the degradation of both cyclin B and securin [13], which occurs at the end of metaphase, was similar in both TTFields- and sham-treated cultures. Staining of microtubule in metaphase cells also appears grossly intact. Because normal exit from metaphase is triggered by the capture of microtubule ends within the metaphase spindle by kinetochores of chromatids that are properly aligned to metaphase plate (see below), our data suggest that metaphase spindle formation and function are unperturbed. However, there was a measurable increase in cells with 4N DNA content following TTFields treatment and persistence in phosphorylated Histone H3 levels, which is usually dephosphorylated in telophase [12, 13]. Further, time-lapse

microscopy of cells stained with a vital DNA dye, allowing the accurate staging of mitosis, revealed that cells treated with TTFields undergo membrane blebbing at the time of metaphase exit [12]. Together, these data strongly suggest that TTFields-treated cells transit normally through metaphase but are disrupted in anaphase due to the violent mitotic blebbing and that leads to aberrant mitotic exit.

TTFields have also been shown to affect the growth of tumor in animal models and human cancers. Treating mice with a number of injected tumors grown from different cell lines including CT26 colon adenocarcinoma, B16/F1 melanoma, Lewis lung carcinoma, F-98 rat glioma, and the highly invasive VX2 carcinoma in rabbits were all shown to undergo tumor regression when TTFields were administered by electrodes placed outside of the body [8, 9, 14, 15]. Interestingly, when the VX2 tumors implanted under the kidney capsule were treated with TTFields delivered only to the abdomen, avoiding the lungs, there was also a marked decrease in lung metastasis compared to sham-treated animals. This suggests that TTFields may have affected either the metastatic potential of the tumor cells, or influenced host immune response against them [14]. These studies demonstrated that TTFields could penetrate the body and affect cellular physiology. This preclinical work led to TTFields testing against human gliomas and a successful phase III clinical trial [16].

Chen et al. [17] also applied similar intermediate frequency of alternating electric fields to B16/F10 melanoma cells both in culture and on tumors developed from flank injection in mice. Their data also showed the inhibition of cellular proliferation in culture and induction of apoptosis in an electrical intensity- and frequency-dependent manner similar to that reported above for TTFields. When they applied these fields to B16/F10 tumors grown in mice they significantly inhibited tumor growth, increased apoptosis by TUNEL staining, and increased mouse survival. Interestingly, they also found that CD34-positive cell numbers were reduced in the treated tumors, indicating an effect on the tumor microvasculature [17]. Beyond being necessary for perfusion of oxygen and nutrients into the tumor bed, tumor endothelium has been implicated in supporting the intratumoral immune inhibitory environment [18, 19]. This suggests that TTFields may target proliferating tumor endothelial cells, and the destruction of these cells may play a major role in contributing to tumor regression.

Basis of Vulnerability to Tumor Treating Fields During Mitosis

Since TTFields affect cells during mitosis, this suggests a specific vulnerability to them may exist in this phase of the cell cycle. The cell cycle is a regimented process that controls cellular growth and proliferation. Biomass accumulation and cellular growth occur during interphase, which is subdivided into G₁, S, and G₂ phases. Non-mitotic and post-mitotic cells exist in a state referred to as G₀. Cell division and daughter cell production occur during mitosis, or M phase, which is further subdivided into prometaphase, metaphase, anaphase, and telophase. During the lengthy period of interphase, enzymatically-driven metabolic processes dominate cellular

behavior with most structural requirements being involved in migration and cell polarization. However, during mitosis, which only lasts approximately 90 minutes in most cultured cells, the dominant cellular processes are almost completely dependent upon the rapid assemblage and function of mitosis-specific protein structures. Unlike the structures that cells depend on during interphase, these mitosis-specific structures require high levels of spatial and temporal precision for their functions. Therefore, while interphase is a highly anisotropic stage, M phase depends on a significant structural ordering at the molecular level in order to achieve successful cell division. This fact likely makes mitosis more susceptible to the electromotive disruption of TTFields than interphase (Fig. 1.1).

The accumulation of newly condensed chromosomes at the midline is dependent on rapid assembly of the highly ordered microtubule structures of the metaphase spindle produced early by the cell after it enters mitosis. During prometaphase, chromosomal material condenses into individually identifiable sister chromatid pairs. In order to migrate to the metaphase plate, the chromatids attach to the metaphase spindle microtubules and move towards the midline through the action of Kinesin motor proteins (Fig. 1.2A) [20]. Once there, the kinetochores within the centromeric regions of each sister chromatid captures microtubules end that are arrayed along the central plane of the dividing cell. This ensures that all chromatid pairs are aligned on the metaphase plate with their constituent kinetochores oriented towards the respective pole of each forming daughter cell. This is necessary to ensure the inheritance of a full complement of chromosomes in each daughter cell. The capture of the microtubules by the paired kinetochores creates physical tension between them that terminates the signals responsible for preventing premature metaphase exit [21]. Since a single pair of unattached kinetochores generates sufficient signal to prevent metaphase exit, the capture of the last kinetochore is required for mitotic progression from metaphase to anaphase. Final kinetochore capture triggers mitotic exit by permitting the rapid and irreversible activation of the anaphase promoting complex (APC/C) ubiquitin ligase activity (Fig. 1.2B). Active APC/C targets the G₂ Cyclin, Cyclin B, and Securin for destruction. Cyclin B is the allosteric activator of the Cyclin-dependent kinase 1 (CDK1) whose activity initiates mitosis and drives cells into metaphase while simultaneously inhibiting processes necessary for anaphase. Securin acts to inhibit the protease Separase that cleaves the Cohesin protein complexes. This cleavage, along with CDK1 inactivation is necessary for the sister chromatids at the mitotic plate to separate and migrate towards the poles of their respective forming daughter cells [22]. Since APC/C is only activated following the capture of the last kinetochore, metaphase exit requires proper microtubule spindle formation and function [23].

Within anaphase, two additional highly ordered structures form, perform their precisely choreographed functions, and are then rapidly disassembled. The anaphase central spindle is a structure consisting of two parallel arrays of microtubules that are joined at the newly formed midline and extend away from each other. This structure is developed to perform two vital functions within minutes of entry into anaphase. During this time, the anaphase spindle pushes the newly formed chromosomes towards the poles of the forming daughter cells. At the same time, the mid-

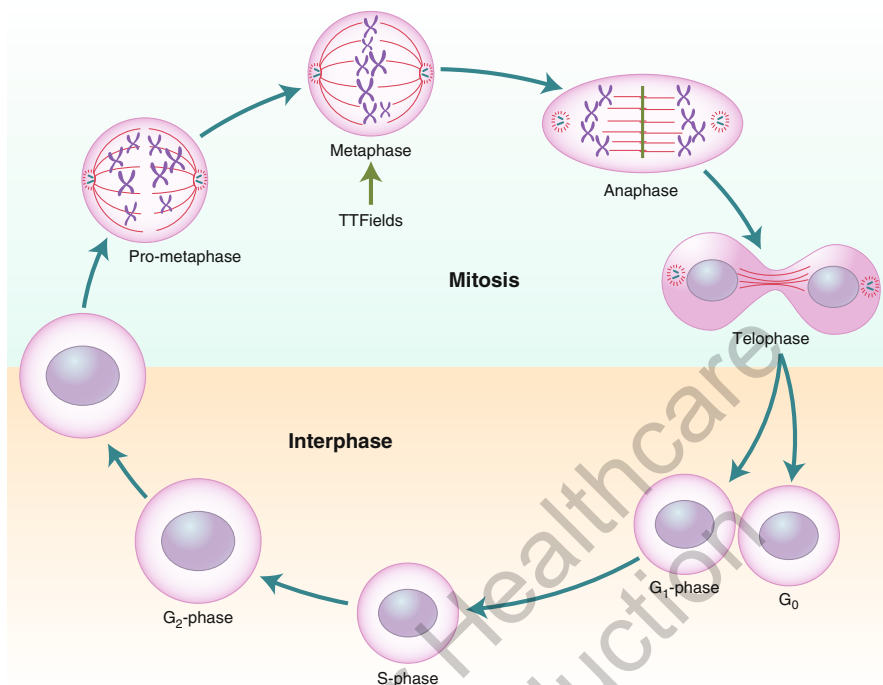


Fig. 1.1 TTFields affect cells during the metaphase to anaphase transition. Dividing cells obtain biomass during interphase and form daughter cells during mitosis. Most of the processes that are essential to cells in interphase are metabolic in nature, many of which function to produce biomass in the form of protein, lipid, and DNA needed for division. On the other hand, mitosis involves the orderly mechanical segregation of daughter chromosomes and division of the parental cell cytoplasm in order to form two independent cells. Mitosis depends on a series of events driven through prometaphase, metaphase, anaphase, and telophase that must be executed with precision in order to ensure that each daughter cell inherits a full and equal complement of the parental genome after it has been duplicated during S phase. Cells that exit mitosis can remain in the cell cycle and enter the G₁ state or exit the cell cycle and enter the G₀ state. The actions of TTFields cause disruption of cells around the time of metaphase exit where the coordination of these mitotic processes is most critical.

line also plays an essential role in the organization and regulation of the third essential mitotic structure, the cytokinetic cleavage furrow (CCF) [24]. This structure contains powerful actinomyosin motor elements that are arranged in a circumference around the equatorial cleavage plane of the dividing cells and is responsible for rapidly cinching the CCF closed during cytokinesis. Significantly, processes within anaphase must be initiated and completed within a short time frame (approximately 10 minutes), and coordinated with each other precisely. This strongly suggests a potential for vulnerability to the electromotive forces generated by TTFields exists during anaphase (Fig. 1.2C). There are a number of proteins within the anaphase spindle midline and the CCF that regulate their organization and contraction, including the centralspindalin complex, composed of KIF23 and MgcRacGAP, which are substrates for phosphorylation by polo-like kinase 1 (PLK1). This phos-

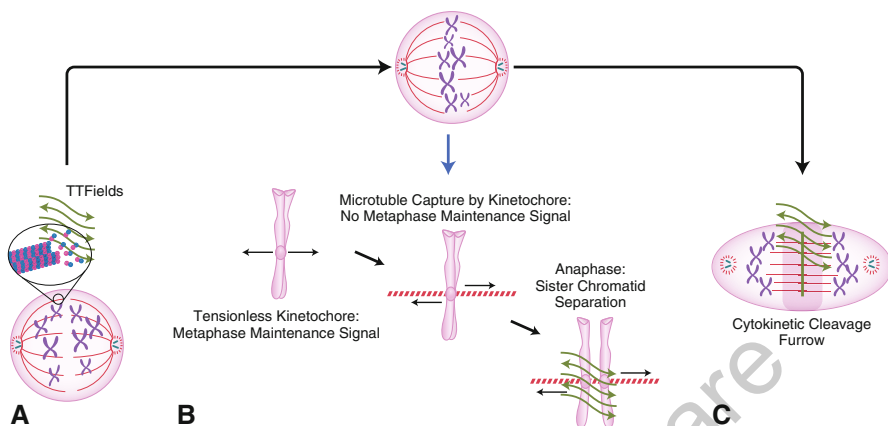


Fig. 1.2 Different stages of mitosis represent different potential points of vulnerability to TTFields. TTFields may perturb mechanically critical processes that are specifically required during mitotic progression, such as the rapid polymerization and/or stability of microtubules in the metaphase spindle (A). The division of sister chromosomes subsequent to kinetochore capture of metaphase spindle microtubules requires the formation of the anaphase spindle, which may also be susceptible to perturbation by TTFields (B). The protein structures that underlay the cytokinetic furrow are also potential targets for TTFields disruption (C).

phorylation creates a binding site for the RhoGEF ECT2 resulting in its recruitment to the spindle midline [25]. ECT2 further binds to the adaptor protein Anillin which in turn binds to the heterotrimeric GTP binding protein Septin 2, 6, 7 complex [26]. ECT2-bound Anillin is required for the stability of the anaphase spindle midline, which becomes disordered upon its depletion [27]. ECT2 is subsequently delivered from the anaphase spindle midline to the CCF, where it is instrumental in directing the localization and regulation of its function during cytokinesis [28]. Upon its recruitment to the CCF, the Septin heterotrimers oligomerize into a highly ordered cytoskeleton-like scaffold that functions to recruit and organize the actinomyosin contractile elements required for furrow ingression and separation of the daughter cells [26, 27, 29–32]. In addition to its function within the CCF, Septins also cross-link F-actin bundles within the submembranous actin cytoskeleton [33–36]. This structure must possess adequate rigidity to withstand the hydrostatic pressures generated by ingression of the cytokinetic furrow. Failure to restrain these forces results in rupture of the connection between cytoskeleton and the overlying plasma membrane which leads to membrane blebbing [33].

Molecular Targets of Tumor Treating Fields

There are several features that a molecular target of TTFields would need to possess in order to produce the observed cellular disruption during mitosis. First, alternating electric fields are likely to act by inducing movement of their molecular targets. This suggests that the presence of high molecular charges on proteins will act to align them

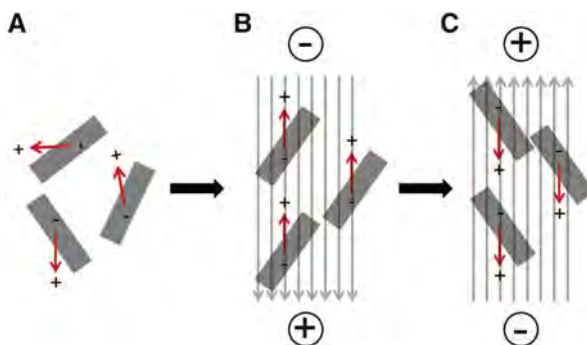


Fig. 1.3 Protein dipole behavior in alternating electric fields. Some proteins possess dipole moments that form positive and negative poles within their structures due to differential densities of positive and negatively charged amino acid residues distributed on their surfaces (A). Within electric fields, the charges on the dipoles are oriented towards the opposite-charged field poles (B). As the poles of an alternating electric field are reversed, the orientation of the dipole containing protein will simultaneously be re-oriented due to the attractive forces imposed by the opposite charges (C).

and possibly induce movement. Proteins possess complex charge structures on their surfaces that arise from the charges of their surface amino acid side chains. The arrangement of acidic and basic residues on the protein surface potentially results in regional separations of surface charges imparting dipole moments onto some proteins, which can be similar to that observed in bar magnets (Fig. 1.3A). Proteins possessing such dipole moments will align within an electric field so that each pole of its dipole will orient towards the oppositely charged pole (Fig. 1.3B). Therefore, the repolarization of the alternating fields is expected to induce a re-orientation to realign the protein dipoles (Fig. 1.3C). Thus, an alternating field would be expected to result in the rotation or induce torsion on intracellular proteins possessing sufficiently high dipole moments, provided that the time constant of rotation or torsion is shorter than the time set for changes in external polarity [9]. Another property that TTFields targets might possess that would explain the ability of alternating electric fields to perturb cell behavior would be the participation of the target protein in the assembly of higher ordered structures. This would result in the electromotive forces exerted by TTFields disrupting cellular process that depends on the integrity of such structures.

Some of the proteins that are critical for the proper progression through mitosis have sufficiently high dipole moments to suggest that they may be affected by TTFields, including α/β -tubulin and the mitotic Septin 2, 6, 7 complex (Fig. 1.4). α/β -Tubulin form the building blocks of microtubules. Taxanes are commonly used chemotherapeutic agents that bind and stabilize microtubules and can cause mitotic catastrophe [37]. The α/β -tubulin heterodimer possesses a high predicted dipole moment of 1660 Debyes (D) (PDB 1JFF, [38, 39]). Therefore, it is possible that TTFields interfere with a critical mitotic function performed by microtubules such as interfering with α/β -tubulin function [8, 9], including the formation and regulation of the metaphase and anaphase spindles [40, 41], or the astral microtubules that are required for CCF regulation [42].

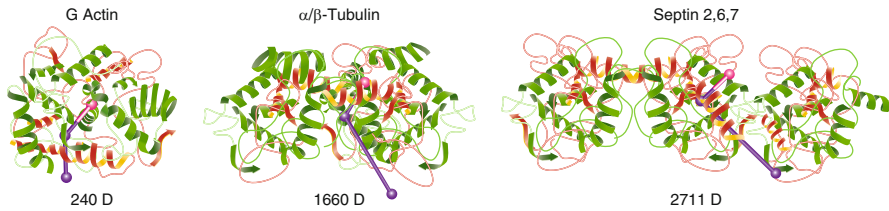


Fig. 1.4 α/β -Tubulin and Septin 2, 6, 7 protein complexes possess high dipole moments. Crystal structures of G-actin, α/β -tubulin, and the Septin 2, 6, 7 complex with superimposed vectors representing the directionality and charge magnitude of their respective dipole moments. G-actin was chosen as a related protein example containing an insubstantial dipole moment.

Heterotrimeric Septin 2, 6, 7 also possesses a high predicted dipole moment of 2711 D (PDB 2QAG, [39, 43]). As described above, this Septin complex is required for functions that are necessary for the later stages of cell division. Septin 2, 6, 7 heterotrimers rapidly polymerize and structurally help to organize and coordinate the CCF activation during anaphase. Once recruited, they then oligomerize and organize the CCF above the equatorial cleavage plane by binding to F-actin filaments and spatially regulate myosin recruitment and activation. Depletion or mutation of ECT2 [44], Anillin [30] or Septin 7 [34] has been shown to result in defective cytokinesis and membrane blebbing. These studies strongly suggest that perturbation of any of the structural/regulatory elements during anaphase leads to aberrant mitotic exit similar to that observed in TTFields-treated cells. Septins also interact with both microtubules and several microtubule interacting proteins that influence microtubule positioning and stability during interphase and mitosis [45]. Therefore, perturbation of either Septin or α/β -tubulin may perturb the function of microtubules. Unlike the cases of cell cycle arrest induced by pharmacologic interventions, such as errors or damages that initiate the G_1/S , G_2/M , or spindle assembly check point (SAC), catastrophic errors that occur after the cell has committed to anaphase are unlikely to be correctable [46].

Supporting the hypotheses that TTFields induce mitotic catastrophe via a perturbation of Septin function, Septin localization to the anaphase spindle midline and cleavage furrow, as well as its reassociation with microtubules upon cell spreading, are significantly perturbed in cells exposed to TTFields [12]. The perturbation of the Septin complex being involved in the cellular response to TTFields is attractive due to its particularly high dipole moment and its known roles during mitosis, including the regulation of CCF function, actin bundle cross-linking, and organization of structures such as the cellular submembranous actin cytoskeleton that is required for its rigidity [33–36]. Further, depletion of Septin 7 by shRNA resulted in membrane blebbing during mitosis [9, 12, 34], as well as an increase in cell size [10, 34], similar to that seen with TTFields treatment. Therefore, this strongly suggests a mechanism of action where TTFields perturb mitosis by interfering with normal Septin localization and function during mitosis leading to membrane blebbing and

aberrant mitotic exit. One of the structural features shared by both the α/β -tubulin heterodimer and the Septin 2, 6, 7 heterotrimer is that the orientation of the dipole moment is predicted to be orthogonal to their longitudinal axis (Fig. 1.4), suggesting that as the polarity of the alternating field reverses, the effect on these proteins will be to induce “pinwheel-like” rotation around a central point within the respective proteins. It is therefore tempting to speculate that inducing such movement on the individual subunits may interfere significantly with their ability to coalesce into their respective higher ordered structures.

Mitotic Effects of Tumor Treating Fields Result in Post-Mitotic Stress

The aberrant mitotic exit induced by TTFields resulted in a high degree of cellular stress, as indicated by increased cytoplasmic vacuoles, decrease in proliferation, and apoptosis [12]. Such aberrant mitotic exit has also been shown to lead to a p53-dependent $G_{0/1}$ cell cycle arrest. This is likely due to a failure to resolve the mitotic spindle apparatus, multiple centrioles, and/or the presence of supernumerary chromosomes [11, 47, 48]. p53-dependent $G_{0/1}$ arrest and apoptosis occurred more than 24 hours after TTFields exposure during mitosis [12]. This suggests the triggering of a p53-dependent mechanism by TTFields in response to mitotic catastrophe and aberrant mitotic exit. These data provide evidence that the efficacy of treatment may be influenced by tumor genetics.

Potential for Immune Involvement in Tumor Treating Fields Mechanism of Action

TTFields may affect patient outcomes in different ways. As described above, TTFields are able to disrupt cells during mitosis and this phenomenon leads to aberrant mitotic exit and cell death. As in the case with spindle poisons, which trigger the spindle assembly checkpoints, cells affected by TTFields exhibit different fates including death in anaphase or aberrant exit from mitosis similar to mitotic slippage [49]. In this way, the mechanism of action may be similar to that proposed for other cancer therapies seeking to destroy tumor cells based on their inherent increased proliferation. This is thought to make them more susceptible to agents targeting dividing cells, such as spindle poisons.

Alternatively, there are several lines of evidence that support a possible immune dependency for TTFields efficacy. Senovilla et al. showed that tetraploid cells that are produced under experimental conditions that perturb mitotic exit exhibit the hallmarks of immunogenic cell death (ICD) [50]. This programmed form of cell death evokes an immune response against the dying cells through cell surface

expression of the endoplasmic reticulum chaperone protein, Calreticulin, and the secretion of the cytokine/alarmins, HMGB1, and ATP [51, 52]. When injected into mice, these dying cells produced a protective immunization against subsequent challenge with the same tumor cell line [50]. Additionally, it has been recently demonstrated that cells made tetraploid by pharmacologic manipulation also express NKG2D and DNAM ligands on their surfaces that act to provoke their clearance by NK cells [53]. Cells that are exposed to TTFields have been shown to also exhibit cellular responses that are consistent with ICD including the cell surface expression of Calreticulin and secretion of HMGB1 [13]. Kirson et al. [14] showed that a brief 5-week TTFields treatment of subrenal capsule injected VX2 tumor in rabbits markedly reduced subsequent metastatic spread to the lungs. Examination of metastatic tumors in the lungs of these TTFields-treated rabbits showed a significant increase in immune infiltrates. This likely indicates a requirement for increased immune protective stroma for tumors that are capable of developing in these animals [14]. In the pivotal EF-11 trial that led to U.S. Food and Drug Administration approval for TTFields treatment of recurrent glioblastoma [16], response typically occurred 6.6–9.9 months following the onset of treatment at which point responders exhibited rapid tumor regression [54]. This pattern of delayed response is also consistent with an immune mechanism of tumor rejection. Finally, clinical data strongly suggest that the use of dexamethasone, a potent immunosuppressive agent, is correlated with patent outcome. Subjects receiving higher than 4.1 mg per day survived significantly shorter than those with lower doses and only subjects in the EF-11 trial who met these criteria responded to treatment [54, 55].

Summary

TTFields likely function by exerting electromotive force on intracellular proteins that both possess sufficiently high dipole moments to be affected by them and are required for critical mitotic functions. Cells exposed to TTFields during mitosis exhibit catastrophic membrane blebbing around the time of metaphase exit resulting in failure within anaphase. TTFields are able to interfere with either structural integrity and/or function of critical proteins necessary for mitotic progression. Once cells become compromised in anaphase, they are unable to exit mitosis normally and slip out of mitosis in the absence of division. Such cells are deranged and nonviable and this can trigger an immune response against them (Fig. 1.5). More research is required to translate these basic science observations into improving the clinical efficacy of TTFields for cancer treatment.

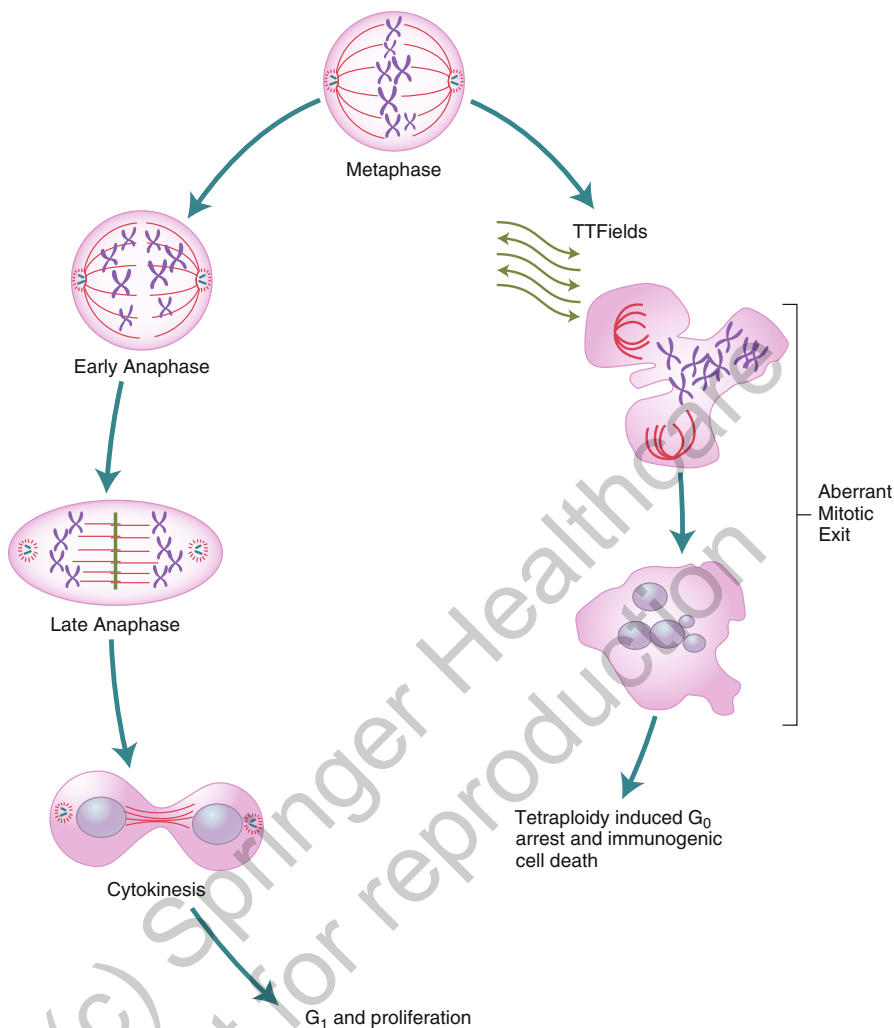


Fig. 1.5 Model for cellular mechanism of action of TTFields. TTFields affect mitotic cells during anaphase resulting in membrane blebbing that perturbs cells during anaphase. This causes a failure of mitotic cleavage and aberrant exit from mitosis. Cells then enter G₀ arrest and progress to immunogenic cell death.

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Chapter 2

Fundamental Physics of Tumor Treating Fields

Edwin Lok and Erno Sajo

Glioblastoma is one of the deadliest forms of brain tumor in humans, yielding a devastating and short survival of only 1 to 2 years [1]. Numerous treatment modalities have been made available to patients over the years to treat this terrible disease, often with only marginal prolongation of survival with a concomitant reduction of quality of life over the course of treatment and in many cases until death. In recent years, collaborative efforts at numerous institutions have been undertaken to investigate a novel noninvasive treatment using alternating electric fields, also known as Tumor Treating Fields (TTFields), and through randomized clinical trials this therapy has been shown to offer a survival advantage in patients with glioblastoma [2–4]. In some of the patients, TTFields were able to reduce tumor size and produce a radiologically visible response [5, 6]. Unlike conventional ionizing radiation, TTFields generated by the Optune® device do not induce direct damage to biomolecules, such as the DNA of the tumor as well as DNA of normal tissues [5, 6]. Also, in contrast to chemotherapy, the device generates electric fields targeting tumor regions, and enables the patient's own immune system to destroy actively dividing glioblastoma cells [7–9].

In order to better understand the clinical and biological effects of TTFields, this chapter is devoted to addressing the fundamental physics that governs these electric fields as generated by the Optune® device. Although a background in physics and mathematics is not required, having such will benefit the readers of this chapter and help them gain an appreciation for the data presented in subsequent chapters.

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The Fundamental Physics of Tumor Treating Fields

The biophysical effects of TTFields are governed by the fundamental laws of electricity and magnetism, namely Coulomb's law, Gauss's law, Ohm's law, and the continuity equation. The dynamic formulations of these laws (also known as electrodynamics) are different from the static versions (as in electrostatics) and they are important to our understanding of how TTFields, which are alternating electric fields at 150 to 200 kHz, induce mitotic disruption in cancer cells and antitumor effects in patients. While the Optune® device generates TTFields by two pairs of orthogonally positioned transducer arrays placed onto the surface of the patient's scalp, the degree of penetration and distribution of these fields from the scalp surface, passing through the calvarium, and into the brain depend on the local tissue properties including their electric conductivity (the ability to pass charges) and relative permittivity (the ability to hold charges) [9]. This is based on Gauss' law, Ohm's law, and the continuity equation that govern the electric field distribution in the human head. First, Coulomb's law describes the electric field strength at a test point located at a distance from a charge located in space and time (Fig. 2.1). Specifically, the field strength decreases in an inverse proportion to the square of the distance or $\frac{1}{r^2}$ from the charge, where r is the radial distance between the test point and the charge.

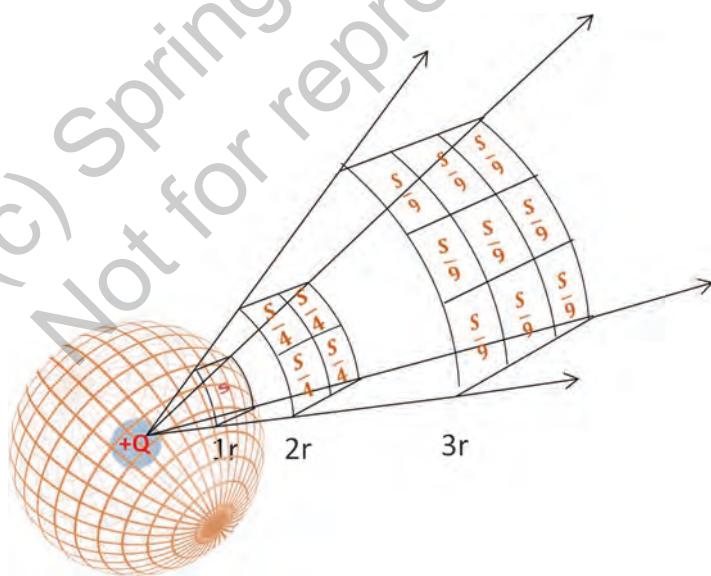


Fig. 2.1 Coulomb's law expresses that the electric field strength drops off with the square of the distance between the charge and a test point in space.

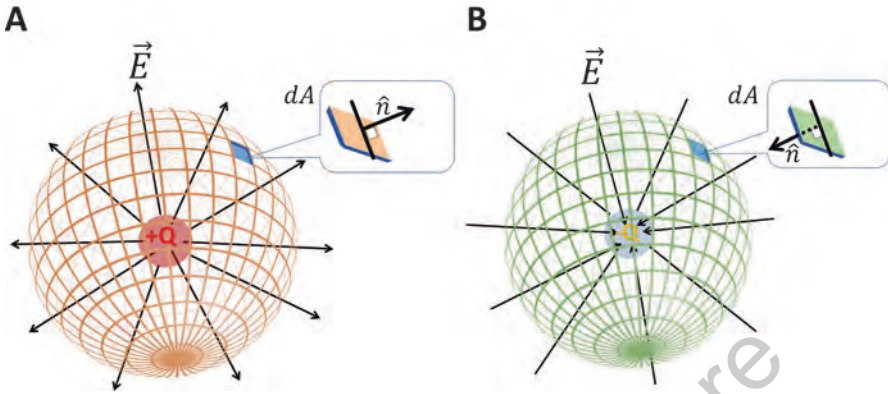


Fig. 2.2 Gauss' law states that the electric flux Φ_E or the flow of electric field is equal to the net sum of the varying electric field \vec{E} over a closed surface area in a volume that encloses all the charges, Q . Here, \hat{n} represents the surface normal through a surface element dA . (A) The electric field lines generated by a positive point charge emanate from the center of the charge and impinge upon a Gaussian surface in an outward direction by convention. (B) The direction of electric field lines of a negative point charge point inward towards the center of charge by convention.

Gauss' law (Eq. 2.1a or Eq. 2.1b) can be derived from Coulomb's law, and it gives the relation between the electric charge and the electric field:

$$\nabla \cdot \vec{E} = \frac{\rho}{\epsilon} \quad (2.1a)$$

$$\Phi_E = \oint (\vec{E} \cdot \hat{n}) dA = \frac{Q_{\text{enclosed}}}{\epsilon_0} \quad (2.1b)$$

Gauss' law mathematically states that the divergence of the electric field, \vec{E} , is proportional to the space charge density ρ and inversely proportional to the permittivity of tissue or media ϵ , which is traversed by the electric charge. Correspondingly, the divergence of \vec{E} is the magnitude of electric field that passes through a cross-sectional area. When Gauss' law is written in its integral form (Eq. 2.1b), it states that the electric flux Φ_E or the flow of electric field is equal to the net sum of the varying electric field \vec{E} , over a closed surface area in a volume that encloses all the charges, Q (Fig. 2.2). Here, \hat{n} represents the surface normal through a surface element dA . Consequently, since the electric field is dependent upon the quantity of charge Q , it is also equal to the total charge enclosed divided by the permittivity of free space ϵ_0 . Therefore, the magnitude of TTFields that traverses through various tissues in the brain, including the tumor, will change depending on the charge density and dielectric properties of the tumor and surrounding tissues.

Ohm's law (Eq. 2.2) is just as important as Gauss' law in determining the penetration and distribution of TTFields due to differences in the electrical properties of intracranial tissues. Ohm's law establishes that the electric current (I) is inversely

proportional and dependent on the tissue's electric resistance (R) at a particular electric potential or voltage (V). The differences in resistance will vary according to the magnitude of the dielectric property of the tissue that the electric field traverses. It is possible to generalize Eq. 2.2 by replacing (1) the current, I , with the current density, \vec{J} ; (2) the inverse of the electric resistance, R , with the tissue-dependent conductivity, σ ; and (3) the electric potential with the electric field \vec{E} (Eq. 2.4). This is made possible by satisfying Poisson's equation for electrostatics (Eq. 2.3), which states that the electric field is equivalent to the negative spatial gradient of the electric potential field ϕ . Hence, the greater the change in electric potential results in a more intense electric field. Since the change in electric potential on the surface of the scalp is significantly higher than that in intracranial tissue, scalp tissue therefore encounters a stronger electric field:

$$I = \frac{V}{R} \quad (2.2)$$

$$\vec{E} = -\nabla \phi \quad (2.3)$$

$$\vec{J} = \sigma \vec{E} \quad (2.4)$$

Finally, the continuity equation describes the conservation of charges within a defined volume, where the divergence of electric current density \vec{J} that passes through a cross-sectional area is equal to the loss of charge density from the volume over time (Eq. 2.5a). Loss of charge here may be interpreted as the negative rate of change in charge density over time, while a gain of charge is interpreted as the positive rate of change in charge density over time. This establishes the basis for charge conservation where charge is neither created nor destroyed. The continuity equation is a critical consideration for the computer modeling of electric field distribution within the brain, and this type of simulation provides the treating clinician a visualization of TTFIELDS distribution in relation to the position of the glioblastoma [10]. Therefore, in this process, specifying the boundary conditions where charges are neither destroyed nor created is an important prerequisite:

$$\nabla \cdot \vec{J} = -\frac{\partial \rho}{\partial t} \quad (2.5a)$$

$$\nabla \cdot (-\sigma \nabla \phi) = -\frac{\partial \rho}{\partial t} \quad (2.5b)$$

Utilizing Eqs. (2.3) and (2.4) the current density may be replaced by $-\sigma \nabla \phi$, yielding Eq. 2.5b. Further, for alternating fields the tissue conductivity is related to the frequency-dependent permittivity, $\epsilon(\omega)$, which will be discussed later in the chapter. The right-hand side of Eq. 2.5 may be set equal to 0 if it is assumed that the induction of electric currents by magnetic fields is negligible. This is known as the quasi-static approximation, which may be valid under the assumption that the wavelength

of the applied field is much larger than the dimension of the object it traverses, i.e., the human brain [11–17]. In this way, many research groups using 10 kHz have assumed that $\partial\rho/\partial t=0$ over a finite time step. Based on the dimensional argument, it appears that this approximation should be still valid at 200 kHz. However, a more rigorous solution that accounts for capacitive tissue effects and the brain’s innate electric fields is to use the full Maxwell equations to solve for the electric field.

Special Considerations for Time-Varying Properties of Tumor Treating Fields

Direct current implies an electric potential across a closed circuit that is constant over time, while alternating current implies a varying potential over an interval of time once the circuit is closed. For the purpose of describing the physical mechanism of TTFields action, we will only describe the applied electric potential by a standard sine wave as a function of time with no phase shift, where $\phi = 0$ (Eq. 2.6 and Fig. 2.3):

$$V(t) = V_{pk} \sin(2\pi ft + \phi) \tag{2.6}$$

V_{pk} is the peak amplitude or peak voltage, f is the frequency, and ϕ is the degree of phase shift. In order to compare the relative strength of different sinusoidal waves with different peak voltages, frequencies, and other parameters, the root mean

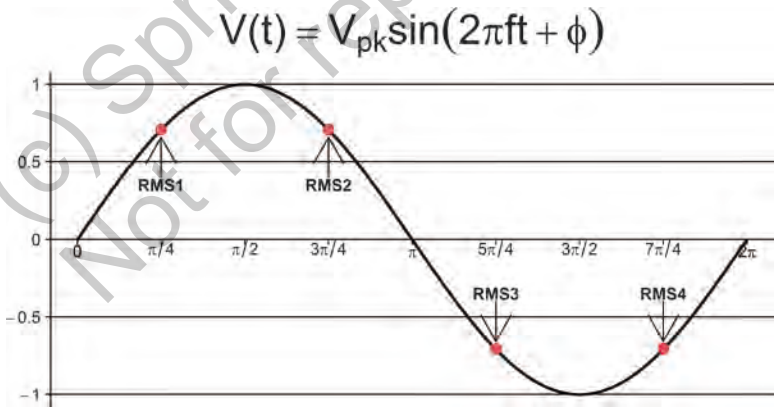


Fig. 2.3 In order to compare the relative strength of different sinusoidal waves with different peak voltages, frequencies, and other parameters, the root mean square (RMS) value is most relevant because this is regarded as the average value of waveforms with alternating characteristics. For the sinusoidal voltage function $V(t) = V_{pk} \sin(2\pi ft + \phi)$, where V_{pk} is the peak amplitude or peak voltage, f is the frequency, and ϕ is the degree of phase shift, there are four RMS values, denoted as V_{RMS1} , V_{RMS2} , V_{RMS3} , and V_{RMS4} .

square (RMS) value is most relevant because this is regarded as the average value of waveforms with alternating characteristics. The RMS value is defined as the value of the amplitude divided by $\sqrt{2}$. For the Optune® device, the electric fields that are generated consist of a continuous sinusoidal wave and, therefore, the RMS and peak-to-peak electric potentials are the most important voltage values on the curve.

The Optune® device by design produces a peak amplitude of roughly 50 V, operates at a frequency of 200 kHz, and has no phase shift. By definition, this sinusoidal function has four specific time points in one complete cycle during which the absolute value of the electric potential is at the RMS or average value. Because the definition of the RMS value for a sine wave is the amplitude divided by $\sqrt{2}$, the four time points for the RMS value can be derived by specifying Eq. 2.6 with a peak voltage of 50 V to solve for t :

$$\frac{50}{\sqrt{2}}(V) = 50(V) \cdot \sin(2 \cdot \pi \cdot f(Hz) \cdot t(s) + 0) \quad \text{Step 1.}$$

$$t_{RMS} = \frac{\sin^{-1}\left(\frac{1}{\sqrt{2}}\right)}{2\pi f} \quad \text{Step 2.}$$

The term $\frac{\sin^{-1}\left(\frac{1}{\sqrt{2}}\right)}{2\pi}$ yields exactly $\frac{1}{8}$, indicating that the RMS value of the electric potential occurs at every $\frac{a_n}{8f}$ for $a_n = 2n - 1$ with $n = 1, 2, 3, 4$ per cycle. By inspection, the peak electric potential is irrelevant when solving for t_{RMS} simply because it was cancelled out before reaching step 2. This clearly shows that t_{RMS} is a characteristic of the frequency of the sine wave. This method is considered a simple and effective way for acquiring the four t_{RMS} time points in any one cycle of the applied sine wave. These four t_{RMS} time points are critically important for the visualization of the electric field distribution in the brain by computer modeling. The set of values below corresponds to the four generalized time points used to compute V_{RMS} for a frequency of 200 kHz and a peak voltage of 50 V:

$$V_{RMS1} = 50(V) \cdot \sin\left(2 \cdot \pi \cdot f(Hz) \cdot \left(\frac{1}{8 \cdot 200,000}\right)(s) + 0\right) \cong 35.356V$$

$$V_{RMS2} = 50(V) \cdot \sin\left(2 \cdot \pi \cdot f(Hz) \cdot \left(\frac{3}{8 \cdot 200,000}\right)(s) + 0\right) \cong 35.356 V$$

$$V_{RMS3} = 50(V) \cdot \sin\left(2 \cdot \pi \cdot f(Hz) \cdot \left(\frac{5}{8 \cdot 200,000}\right)(s) + 0\right) \cong -35.356 V$$

$$V_{RMS4} = 50(V) \cdot \sin\left(2 \cdot \pi \cdot f(Hz) \cdot \left(\frac{7}{8 \cdot 200,000}\right)(s) + 0\right) \cong -35.356 V$$

Capacitive Response of Biological Tissues to Tumor Treating Fields

An accurate analysis of biological tissue response to the applied TTFields requires an understanding of the physical characteristics of a capacitor, which consists of a medium (also known as a dielectric) that retains charge over time. The dielectric medium may be any insulator material placed between conductive interfaces where charge is stored. Often, conductive media are associated with metals or metallic materials while insulators are likened to nonmetals, such as glass or air. However, when we rigorously analyze their properties, in practice they are neither perfect conductors nor perfect insulators. A perfect insulator essentially has the property where no electric charge or current may traverse through the material and thus its conductivity is equal to zero. By Eq. 2.4, the current density in this medium is 0 and therefore the electric field is 0 as well. Of course, in the real world any material considered an insulator has a finite threshold for dielectric breakdown, which occurs when a sufficiently high electric potential is applied across the medium at which it can no longer prevent charge transport. A classic example of this phenomenon would be lightning strike through air. When the electric field between the surface of the Earth and clouds in the atmosphere is large enough, the air's property as an insulator between the two interfaces temporarily breaks down due to a partial and propagating ionization of the gas from very high electric stress and thus a visible lightning strike is seen. The partial ionization of the gas can be explained further by considering that the potential energy applied across the gas exceeds the maximum threshold of the insulating capacity, which is defined by the dielectric strength of the gas medium. When saturated with charge, the insulator will momentarily act as a conductor, releasing a surge of energy where the charges flow to the ground at a near instant.

As the Optune® device applies a voltage across the head with a peak voltage of 50 V, there will be variations in the electric field distribution intracranially due to difference in material composition within different structures that are neither a perfect insulator nor a perfect conductor. Two important dielectric properties to consider are the electric conductivity (σ) and relative permittivity (ϵ). In general, the electric conductivity is derived from the electrical resistivity, and it governs the magnitude of the current density \vec{J} for a uniformly applied electric field as previously described in Eq. 2.4. Specifically, the electric conductivity is the inverse of the electric resistivity. In the case of time-varying or alternating electric fields, the relative permittivity is a complex parameter (with real and imaginary parts); it is a function of the angular frequency and is referenced to the permittivity of vacuum or that of free space ϵ_0 as seen in Eq. 2.1b. Equation 2.7a shows the relative permittivity as a function of the alternating field's angular frequency (ω) written in both the real and imaginary parts, where $i = \sqrt{-1}$ and $\omega = 2\pi f$. A more realistic way of expressing Eq. 2.7a is one that forms a relationship between the relative permittivity and conductivity for linear isotropic materials, as Eq. 2.7b does:

$$\varepsilon_r(\omega) = \varepsilon_r'(\omega) + i\varepsilon_r''(\omega) \quad (2.7a)$$

$$\varepsilon_r(\omega) = \varepsilon_r'(\omega) + i \frac{\sigma}{\omega \varepsilon_0} \quad (2.7b)$$

Unfortunately, biological tissues invariably exhibit nonlinear anisotropic behaviors, where Eqs. 2.7a and 2.7b must be modified and thus the relative permittivity stems from a generalized dielectric relaxation model as given by the Cole-Cole equation, Eq. 2.8 [18–20]:

$$\varepsilon_r(\omega) = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + (i\omega\tau)^{1-\alpha}} \quad (2.8)$$

Here, ε_∞ and ε_s are the infinite-frequency and static permittivities, respectively, and τ is a time constant. α is the spectral shape parameter with values between 0 and 1 (Debye model). Real-world materials, including biological tissue, are dielectrics that to some extent have bound charges forming neutral atoms. When an electric field is applied, the material will become polarized proportional to the polarization density \vec{P} . These bound charges distort the electric field in the medium due to a retarding effect that is dependent on the dipole moments and the electric susceptibility of materials χ_e , which describes the ability of a dielectric to be polarized (Fig. 2.4). It should be noted, however, that for anisotropic medium, χ_e is a tensor, a quantity written in a matrix form that expresses both its magnitude and direction. For linear homogeneous isotropic dielectrics, the polarization density is related to the electric field and it can be written as a function of time, as in Eq. 2.9a, or as a function of frequency, as in Eq. 2.9b:

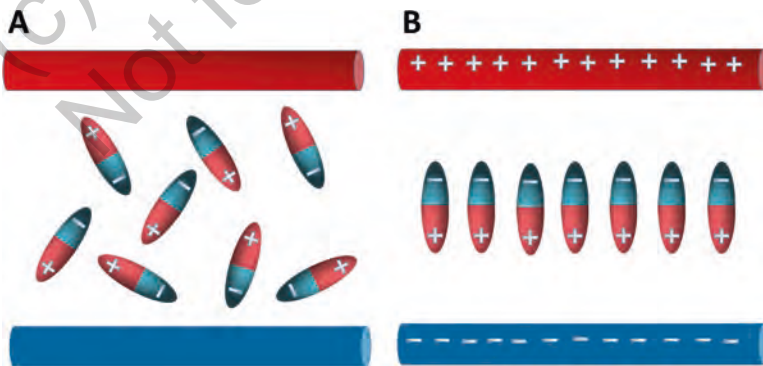


Fig. 2.4 When an electric field is applied, the dipoles in (A) will become polarized proportional to the polarization density and align in a parallel fashion as in (B) to the applied electric field.

$$\vec{P}(t) = \epsilon_0 \int_{-\infty}^t \chi_e(t-t') \vec{E}(t') dt' \quad (2.9a)$$

$$\vec{P}(\omega) = \epsilon_0 \chi_e(\omega) \vec{E}(\omega) \quad (2.9b)$$

Finally, the electric displacement field \vec{D} , which relates to the polarization density and the electric field, may be written in the frequency domain as in Eq. 2.10:

$$\vec{D} = \epsilon_0 \vec{E} + \vec{P} = \epsilon_r \epsilon_0 \vec{E} \quad (2.10)$$

By subtracting the effect of bound charges on the dielectric from the total electric field \vec{E} , the effect from free charges can be described as a function of the applied electric field across the dielectric. This is particularly useful to delineate the behavior of a dielectric medium in the presence of an external electric field.

Another important concept to consider about capacitors is that the charging and discharging characteristics do not change when operating either in direct or alternating current. However, this characteristic of the medium's dielectric properties affects the time constant of the material, which in turn affects the dielectric medium's response to the flow of electric current. This particular response is known as capacitive reactance, where the time constant is a way to describe the time it takes for charges within a medium to relax or approach electrostatic equilibrium (Eq. 2.11):

$$\tau = \frac{\epsilon}{\sigma} \quad (2.11)$$

Materials with large time constants take a longer time for charges to approach electrostatic equilibrium, while those materials with a smaller time constants require a shorter duration. Interestingly, but not surprisingly, the time constant of a medium is frequency dependent and will change as the frequency of the applied alternating electric current changes. Equation 2.12 is the standard solution of a first-order homogeneous differential equation describing the discharge of a capacitor [19, 20]:

$$V(t) = V_0 e^{-\frac{\sigma}{\epsilon} t} \quad (2.12)$$

For the purpose of exploring the differences of various tissue types within the brain, we consider a solved patient brain dataset with the respective dielectric properties applied, shown in Fig. 2.5A, exposed to a 200 kHz wave as the TTFields are programmed to emit through the arrays. After applying the appropriate dielectric properties of the various segmented tissues in the head, the model is solved. The cerebrospinal fluid (CSF) is mostly aqueous, mixed in with a variety of proteins and salts as it serves as a conduit between the central nervous system and the brain. Gray matter is composed mostly of lipids, behaving electrically more like an insulator or a material with a larger dielectric constant relative to CSF. Since the CSF in this

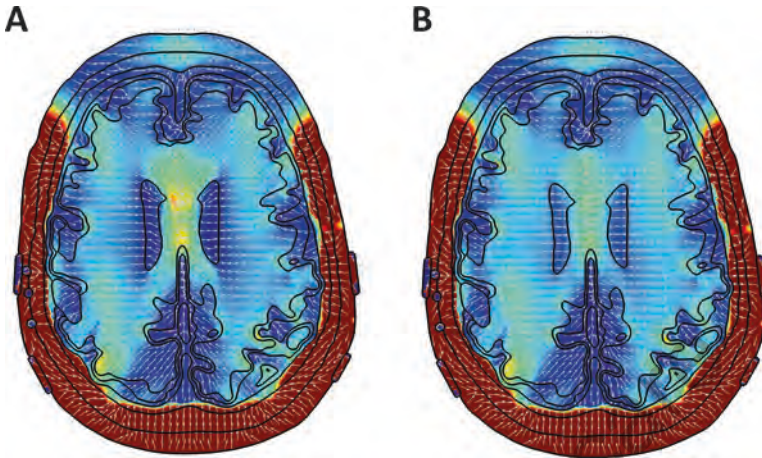


Fig. 2.5 The effect of the highly conductive CSF compared to surrounding gray matter tissue with lower conductivity causes changes to the electric field distribution in the brain. (A) The electric field in the region between the bilateral ventricles, which are filled with CSF, experiences a higher intensity due to the relatively large conductivity difference compared between CSF and gray matter. (B) The electric field in the region between the bilateral ventricles when gray matter dielectric properties are applied to the bilateral ventricles evens out the differences in conductivity as in A and thus the field intensity is reduced. Note that the white vectors that overlay both maps, representing the direction of the electric field, are essentially pointing in the same direction and the magnitude of the electric fields is different between the two cases. CSF cerebrospinal fluid

example is more conductive than the block of gray matter in between, it would serve as the conductive terminals of a capacitor, while the gray matter in between would serve as the dielectric medium. The accepted isotropic electric conductivity of CSF and gray matter at 200 kHz is about 2 S/m and 0.141 S/m, respectively, while the accepted relative permittivity for CSF and gray matter at the same frequency is about 109 and 2010, respectively [21]. It has been shown that conductivity plays a greater role than permittivity in altering the distribution of TTFields within the brain [9, 22, 23].

In a modified model of the same brain dataset as described in Fig. 2.5A, when the dielectric properties of the bilateral ventricles are replaced with the gray matter dielectric properties, it can be observed that the electric field distribution in the region between the bilateral ventricles is vastly different (Fig. 2.5B). By applying TTFields in both constructs simultaneously, the electric potential will rise to a fully charged state at a much faster rate when CSF in the bilateral ventricle acts as the dielectric medium of a capacitor compared with gray matter as the dielectric. Similarly, when the electric potential source is disconnected from both capacitors after being fully charged, the discharging of both capacitors will commence. Once again, the capacitor with the CSF as a dielectric medium will discharge, or approach electrostatic equilibrium, at a faster rate than the capacitor with the gray matter as the dielectric. This ability for a medium to charge and discharge can be expressed as capacitive reactance,

which is the resistance to change in electric potential in a capacitor (Eq. 2.13), where f is the frequency of the applied electric potential and C is the capacitance:

$$\chi = \frac{1}{2\pi fC} \quad (2.13)$$

For a constant direct current, which does not vary with time, the frequency component is 0, and therefore reactance does not apply. However, when an alternating current is applied as the electric potential source, there exists a frequency component that affects the ability of a capacitor to hold and retain charges over a cycle. For instance, from the example described in Fig. 2.5, when an alternating current is applied across either capacitor at 200 kHz, the only term left in Eq. 2.13 that determines the opposition to change in electric potential is the capacitance, which is inversely proportional to the capacitive reactance. Likewise, a lower capacitance results in a higher capacitive reactance or greater opposition to change in electric potential. Therefore, since CSF is more conductive than gray matter, CSF cannot retain enough charge to reach full potential before the field collapses and changes polarity.

Specific Absorption Rate in Tissue from Tumor Treating Fields

An important and relevant quantity to the discussion of TTFields is the specific absorption rate (SAR), which is the amount of power absorbed by a unit mass of tissue (Eq. 2.14), where σ is the conductivity of the inquired tissue, \vec{E} is the electric field, and ρ is the physical density of tissue. Power is defined as the change in energy over time and since TTFields are applied continuously over a long period of time, it is appropriate to quantify the amount of energy deposited in tissue in terms of power. Similar to the energy per unit mass of tissue as deposited by ionizing radiation that is expressed as dose in gray or J/kg, the rate of energy or power deposited by TTFields can be expressed as SAR or in W/kg. In computer modeling of electric fields in the brain, the delineation of SAR may help determine the amount of energy deposited over time at the tumor or other intracranial regions of interest:

$$SAR = \frac{\sigma |\vec{E}|^2}{\rho} \quad (2.14)$$

Conclusions

An understanding of the basic physics principles of electricity and magnetism is of utmost importance to appreciate and learn more about the biophysical interactions within the brain induced by external electric fields applied on the surface of the

scalp. The fundamental principles that govern TTFields include Coulomb's law, Gauss' law, Ohm's law, and the law of continuity. Derivatives of these equations to account for time-varying TTFields are essential to accurately describe the alternating electric field distribution within the brain during every cycle. Brain tissues are essentially dielectric materials with different conductivity and relative permittivity properties that change the electric field distribution due to their respective capacitive reactance characteristics and thus these distributions are nonuniform. Since TTFields are applied continuously in the patient, a more appropriate physical quantity to describe the amount of energy absorbed in the tissue media may be expressed in terms of power. Therefore, the concept of SAR can be used to describe the amount of power absorbed in a unit mass of tissue over the prolonged period of treatment time. With the fundamental biophysical characteristics established, the nature of TTFields and its probability and types of interaction with different tissues, cells, and subcellular components are then better understood, leading to our ability to further improve and develop this technology to provide better treatment outcomes for patients with glioblastoma and other malignancies.

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Chapter 3

Biophysical Effects of Tumor Treating Fields

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Within the last decades, the effect of applied electric fields on biological cells has been extensively studied. At the cellular scale, different research groups concentrated their efforts on studying a variety of local effects from the electric field, such as the induced transmembrane voltage (TMV) under different stimulation conditions, as well as various single- and multiple-cell properties. The preliminary and most popular studies go back to H.P. Schwan and colleagues who not only analytically described the steady-state TMV induced in spherical cells [1], but also clarified mechanisms responsible for electrical properties of tissues and cell suspensions [2]. These insights were used to estimate the dielectric properties of cells and tissues allowing, for example, impedance measurements to differentiate normal and cancerous tissues [3]. Alongside, possible cell manipulation procedures employing electric fields have been investigated; that is, it was observed that cells may respond to AC polarization by orienting, deforming, moving, or rotating in a frequency-dependent manner [4, 5]. These investigations are applied for manipulation, trapping, separation, or sorting of biological cells or colloidal particles [4, 5].

Cellular scale observations can be translated into medical treatments and applications. The well-known techniques for nerve, muscle, and heart stimulation use DC pulses or very-low-frequency AC fields [6]. This relies on the fact that for frequencies below about 1 kHz, the excitable tissues can be stimulated through membrane depolarization. When the frequency increases, the response of the biological cell membranes is too slow to respond to high-frequency depolarization and thus becomes refractory to further stimulation. On the other hand, effects induced by very-high-

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frequency fields range from heating to membrane disruption, electroporation, and cell death, depending on the field strength [5]. Commonly used medical treatments that utilize fields with frequencies in the high MHz or GHz range are diathermy and radiofrequency tumor ablation. In summary, most of the investigation of the response of cells to AC electromagnetic fields has focused on the low-frequency (<10 kHz) or high-frequency ranges (MHz or GHz). Intermediate-frequency AC electric fields in the kHz to MHz region were long thought to have no meaningful biological effect and are just currently being investigated in more detail [7–12].

One technique that makes use of this intermediate-frequency range is a relatively new modality for cancer treatment termed Tumor Treating Fields (TTFields). This method relies on low-intensity, between 1 and 3 V/cm, and intermediate-frequency, between 100 and 300 kHz, alternating electric fields that have been shown *in vitro* and *in vivo* to destroy selectively dividing cells that are undergoing mitosis and cytokinesis [7, 13–15]. One assumed mechanism of action is an anti-microtubule effect whereby tubulin subunits are forced to align with the applied field, perturbing the formation of functional mitotic spindles that are essential for the completion of mitosis. A second possible mechanism of action relates to a dielectrophoretic (DEP) effect since the cellular morphology during cytokinesis gives rise to a non-uniform intracellular electric field, with a high gradient at the furrow between the dividing cells exerting forces on polar macromolecules and organelles. Preclinical data demonstrated mitotic arrest, and subsequent apoptosis of different cancer cell lines, as well as structural disruption associated with violent membrane blebbing [7]. TTFields treatment spares quiescent cells and specifically targets cancer cells undergoing mitosis, with a particular optimal frequency of largest inhibitory effect for each cell line tested [7, 13, 16].

TTFields are currently used to treat glioblastoma multiforme (GBM) patients. The Optune® system is a medical device that was developed to deliver the TTFields to the brain via transducer arrays placed on the patient's scalp. Following the mentioned *in vitro* experiments, these transducers deliver alternating electric fields of 200 kHz in two perpendicular directions. Optune® was approved for the treatment of recurrent GBM by the U.S. Food and Drug Administration in 2011 [17]. In October 2015, TTFields in combination with temozolomide was also approved for newly diagnosed GBM patients [18, 19].

Computational Cell Models

Although the electric behavior of simple cell morphologies like spheres or ellipsoids can be described analytically, more complex and realistic shapes can only be investigated with the help of computational models. There already exist some studies that specifically investigate the electric field distribution within the quiescent and the dividing cell induced by alternating, intermediate-frequency, low-intensity fields [8, 9, 12]. In all of these studies, the finite element method (FEM) is used to

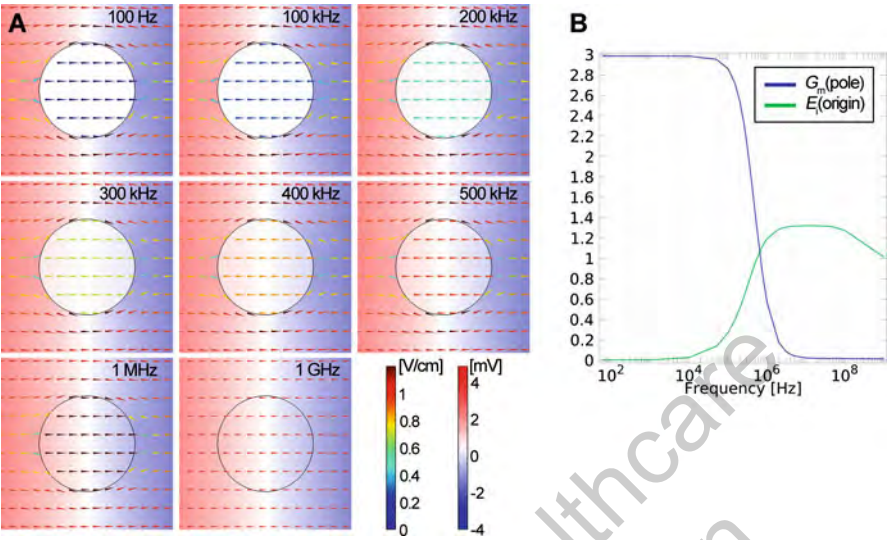


Fig. 3.1 Frequency effect of the electric field on mitotic cell. (A) The electric field is represented by *arrows* with corresponding rainbow color scale (V/cm). Surface plots of the electric potential are also presented (mV). Different frequencies have been selected. (B) Line plots of the membrane field gain at the cell’s pole (*blue*) and the intracellular electric field strength E_i at the origin as a function of frequency. Adapted from Wenger et al. [12].

solve for the electric potential in and around single cells, enabling the calculation of the TMV, i.e., $U_m = \varphi_i - \varphi_e$, and the electric field distribution.

Since the cell rounds up during mitosis [20, 21], it can be represented as a sphere with a very thin membrane with a thickness d_m which separates the intracellular from the extracellular space (Fig. 3.1A). Thus, three domains are distinguished which possess different dielectric properties, i.e., specific values of the electric conductivity σ and the relative permittivity ε (Table 3.1).

The Effect of Frequency on the Electric Field During Metaphase

If an alternating electric field of magnitude E_e is applied to the extracellular space, the magnitude of the resulting electric fields in the membrane, E_m , and the intracellular space, E_i , are frequency dependent. Furthermore, the field inside a homogeneous spherical cell placed in a uniform applied field is also uniform (Fig. 3.1A). In order to examine the frequency dependency of the induced fields some authors plot the (normalized) potential at the cell’s pole against frequency, e.g., [22–24]. Others discuss the membrane field gain G_m , which reflects the frequency-dependent

Table 3.1 Standard, minimum (min), and maximum (max) values of geometric and dielectric properties.

	Unit	Min	Standard	Max	
r_{cell}	[μm]	4	10	15	Cell radius
d_m	[nm]	—	5	—	Membrane diameter
σ_i	[S/m]	0.1	0.3	0.9	Intracellular electric conductivity
σ_e	[S/m]	0.9	1.2	1.2	Extracellular electric conductivity
σ_m	[S/m]	3×10^{-7}	3×10^{-7}	5×10^{-5}	Membrane electric conductivity
ϵ_i		60	72.3	80	Intracellular relative permittivity
ϵ_e		60	72.3	80	Extracellular relative permittivity
ϵ_m		2.5	5	7.5	Membrane relative permittivity

amplification of the applied field in the membrane, and is defined as $G_m(\omega) = \frac{E_m(\omega)}{E_e}$, where ω is the angular frequency [25, 26]. Since the cell membrane is assumed homogenous, the induced membrane electric field can be expressed as $E_m(\omega) = \frac{U_m(\omega)}{d_m}$, and therefore $G_m(\omega) = \frac{U_m(\omega)}{d_m E_e}$.

The values of G_m and thus also E_i certainly change for different frequencies of the applied electric field (Fig. 3.1B). For very low frequencies below about 1 kHz, G_m is constant and high, resulting in almost zero intracellular field strength E_i . As the frequency increases the TMV decreases, the amplification of the membrane electric field is reduced, and the electric field “invades” the cell, increasing its strength E_i . This can be observed in Fig. 3.1B by the descent of the blue G_m curve and the increase of the green E_i curve. The TMV is basically independent of frequency until the angular frequency $\omega = 2\pi f$ becomes comparable with the reciprocal of the time constant:

$$\tau = \frac{r_{\text{cell}} \cdot \frac{\epsilon_m}{d_m}}{\frac{2\sigma_e \sigma_i}{2\sigma_e + \sigma_i} + \frac{r_{\text{cell}}}{d_m} \sigma_m}. \quad (3.1)$$

As has been stated (Eq. 3.1), the limit for low-frequency potential for typical cell sizes ranges from the upper kHz to the lower MHz range. With the standard parameters given in Table 3.1, this breakpoint frequency is 480 kHz, which is exactly the point where the blue line in Fig. 3.1 starts to descend. In the low-MHz region, when this line drops below $G_m = 1$, which marks the region where $E_m < E_e$, the electric field inside the cell becomes higher than the applied field in the extracellular space. Zero values of the field gain G_m signify total uniformity in all domains, with the electric fields equalized to the value of the excitation field, i.e., $E_m = E_i = E_e$.

This behavior is also illustrated in the first column in Fig. 3.1A. Up to 100 kHz the electric field inside the cell, in blue cones, is lower than the field in the extracellular space. As the frequency approaches the breakpoint the intracellular electric field strength starts to increase. At 500 kHz the field strengths inside and outside the cell become equal, and are plotted in orange cones. At slightly higher frequencies, the membrane field gain becomes lower than 1 and the field inside the cell, now in red, becomes higher than that in the outside. The last plot at the bottom right illustrates the convergence to the excitation intensity.

The Effect of Dielectric Properties on the Electric Field During Metaphase

The assumed dielectric properties of the biological media vary between publications. Many computational studies [22, 25, 27–29] concerning similar investigations adopt values for the conductivity and relative permittivity from previous studies [23, 30, 31]. Those values were taken from investigations on yeast cells [32], erythroleukemia cells [33], and T and B lymphocytes [34]. Yet, these parameters are also used for studying neurons [35, 36]. Furthermore, different values may also be expected for glial cells [37–41] and pronounced differences exist between the electrical properties of some cancerous and non-cancerous tissues [5]. Thus, we systematically tested the effect of changing the dielectric properties on the intracellular field strength [8, 12], for the range of values presented in Table 3.1. Figure 3.2 summarizes the most important consequences in the observed electric behavior and plots the intracellular field strength E_i as function of frequency. Increasing E_i is predicted for increasing σ_m without shifting significantly the frequency at which E_i increases most rapidly (Fig. 3.2A). When ϵ_m is increased, E_i also increases with an earlier and faster growth for higher ϵ_m values (Fig. 3.2B). Decreasing E_i is predicted for increasing σ_i with an earlier and faster growth for lower σ_i values (Fig. 3.2C). Changes in σ_e , ϵ_e , and ϵ_i affect E_i only at very high frequencies (Fig. 3.2D).

In summary, the simulations with the spherical metaphase cell predict a uniform intracellular field with nonzero E_i . Depending on cell properties, the frequency window of the predicted transition range might be shifted.

The Effect of Cell Shape on the Electric Field During Telophase

During telophase the two dividing sister cells have elliptical cell shape [20, 21]. The simulations we performed [8, 12] assume three different stages of cytokinesis; that is, two ellipsoids with major radii of 10 μm and minor radii of 7 μm

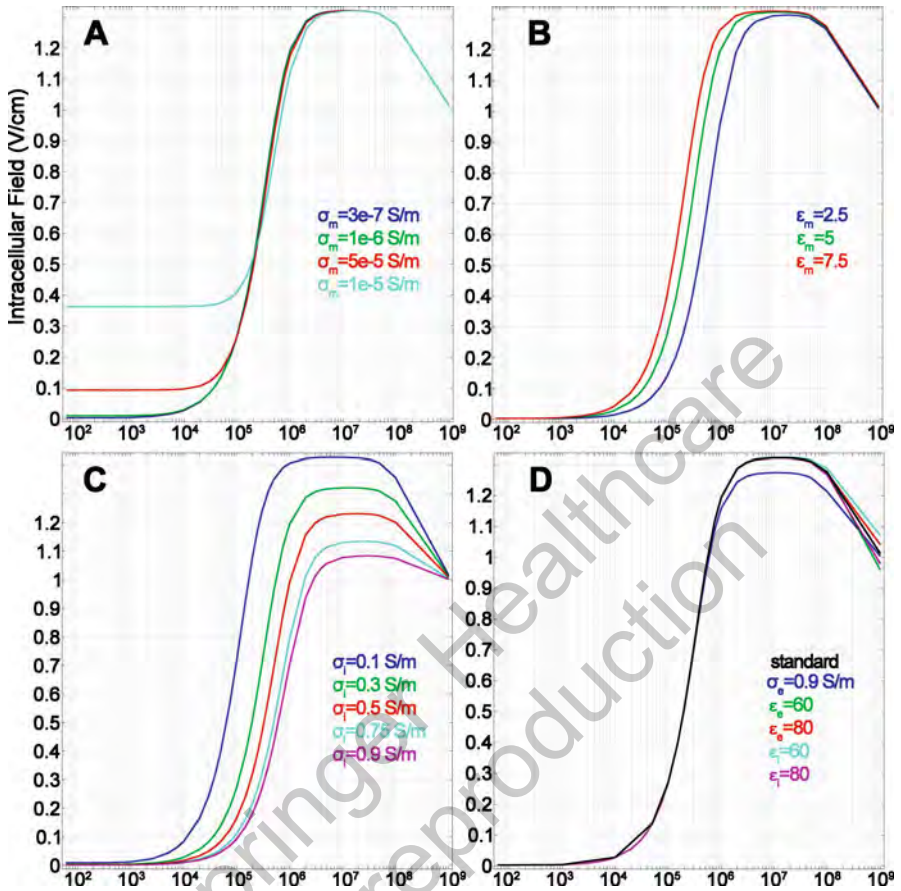


Fig. 3.2 The intracellular field strength E_i at the center of the cell as a function of frequency for varying σ_m (A), ϵ_m (B), σ_i (C), and in σ_e , ϵ_e , and ϵ_i (D). Adapted from Wenger et al. [12].

(minor radius is always 70 % of the major radius) are pulled apart by increasing the distance between the cell centers by 50 %, 90 %, and 99 % of the cell major diameter, respectively (Fig. 3.3). In contrast to what was observed in the spherical metaphase cell, the intracellular electric field is non-uniform and converges towards the cleavage plane separating the two sister cells. Figure 3.3 shows a surface plot of electric field displayed with fixed color range with selected frequencies plotted in rows and cytokinesis stages in columns. Again E_i is almost zero at low frequencies, but field non-uniformity becomes apparent in the low-kHz range. This is particularly visible for later stages of cytokinesis (third and fourth columns in Fig. 3.3) with corresponding maximum E_i values that are much higher than the applied field of 1 V/cm.

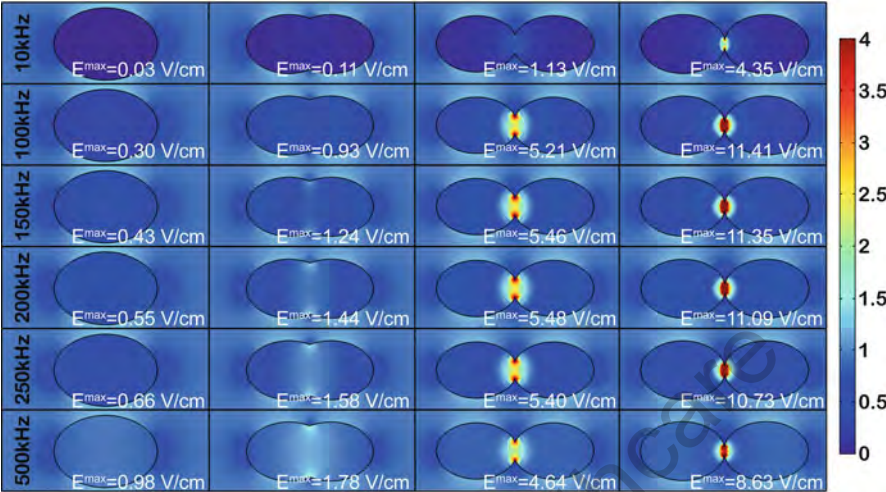


Fig. 3.3 Electric field distribution for selected frequencies (rows) and different stages of cytokinesis (columns). Adapted from Wenger et al. [12].

The right column of Fig. 3.3 with almost separated sister cells shows the most pronounced and spatially confined electric field at the furrow, which is present even for a low 10 kHz stimulation frequency. At higher frequencies, the non-uniformity close to the furrow decreases as the field strength further increases throughout the cell. The highest maximum value of E_i of 11.41 V/cm is predicted for stimulation at 100 kHz, in the last stage of cytokinesis. The furrow between the cells is longer in an earlier stage of cytokinesis depicted in the third column, and the highest maximum value of E_i , 5.48 V/cm, is reached at 200 kHz.

A non-uniform electric field induces unidirectional DEP forces. This DEP force leads to the motion of polarizable particles as a result of the interaction of a non-uniform electric field \mathbf{E} with their induced dipole moment \mathbf{p} , i.e., $\mathbf{F} = \mathbf{p} \cdot \nabla \mathbf{E}$ [42], and it is proportional to the square of the gradient of the electric field, i.e., $|\mathbf{F}| \propto |\nabla \mathbf{E}|^2$ [43, 44]. The term $|\nabla \mathbf{E}|^2$ is referred to as the DEP force component, and has units of V^2/m^3 . In analogy with the observed E_i peaks, also the DEP force component shows stage-specific peak frequencies. This is displayed in Fig. 3.4B where the normalized DEP force component is plotted as function of frequency for the three cytokinesis stages. Well-defined peak frequencies are observed at 450 kHz, 175 kHz, and 125 kHz for stage 1 (orange), stage 2 (green), and stage 3 (blue), respectively. Thus, the peak frequency is decreasing for later stages of cytokinesis, but with increasing absolute force component values.

The reported peak frequency values correspond well with the reported frequency dependence of TTFields [7, 13]. Furthermore the dose dependency of TTFields [7], which relates to the fact that the inhibitory effect of TTFields increases rapidly with

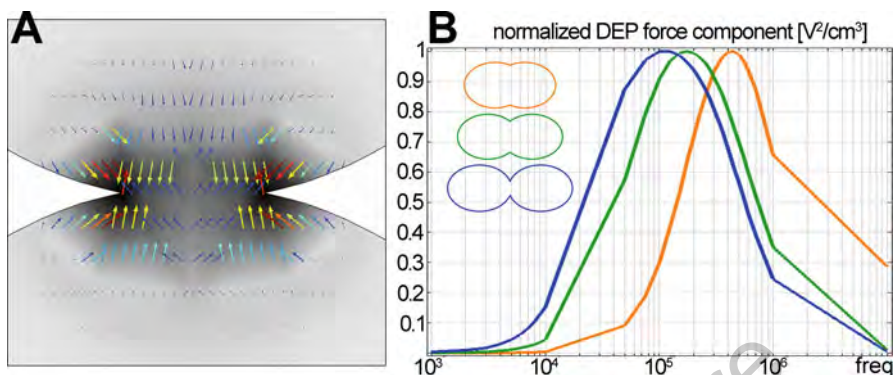


Fig. 3.4 DEP forces on a cell during cytokinesis. (A) Close-up of the furrow region and the DEP force component plotted as *arrows*. (B) The normalized DEP force component for the three stages of cytokinesis. Adapted from Wenger et al. [12].

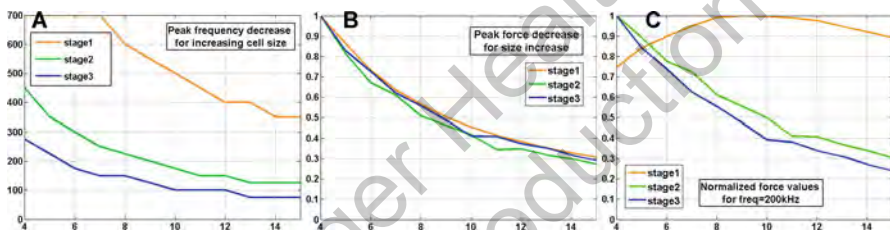


Fig. 3.5 Cellular characteristics that influence DEP forces. (A) The peak frequency (kHz) of maximal DEP force component as a function of cell radius (μ m) for the three stages of cytokinesis. (B) Normalized maximal peak force values, plotted as functions of cell radius. (C) The normalized DEP force component values at 200 kHz for the three stages.

increasing applied field strength, was confirmed by this computational modeling approach [8, 12]. One additional experimentally observed effect was that the optimal frequency for inhibitory effect of TTFields is inversely related to cell size [7, 13], and increased cell volume is seen in almost all cell lines treated with TTFields [45]. Again computational modeling predicted similar results, by repeating the simulations with dividing cells whose major radius ranges from 4 to 15 μ m. Figure 3.5A shows that the peak frequencies (in kHz) of the DEP force component decrease and then level off with increasing cell radius (in μ m). The corresponding maximum values of the DEP force component also decrease for increasing cell size, but the normalized decay rate is the same for all cytokinesis stages (Fig. 3.5B). Consequently, for a constant 200 kHz TTFields frequency, smaller cells in late cytokinesis are exposed to higher force (Fig. 3.5C). This indicates that a larger cell might be less affected by the field.

Conclusion

This comprehensive description serves as a first approach to further elucidate the details behind the mechanisms of action of TTFields, and more generally to provide a deeper understanding of the electric field distribution within cells under the influence of alternating electric fields. It also illustrates how computational modeling can be used to systematically investigate the effect of changes in cell physical properties, shape, and size on the intracellular electric field. Future insights into the biophysical effects of alternating electric fields may be gained through computational modeling at the subcellular level or at the level of cell assemblies.

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Chapter 4

Computer Simulation of Tumor Treating Fields

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Tumor Treating Fields (TTFields) use frequency-tuned alternating electric fields at 200 kHz that disrupt tumor cells as they undergo mitosis. The targets of these fields are proteins such as α/β tubulin and septin that have high dipole moments. In the patient, TTFields are applied on the scalp by two pairs of orthogonally positioned transducer arrays. Because the energy delivered by TTFields is relatively low, the electric field is spatially distorted by variations in the local conductivity and relative permittivity of tissues and fluid cavities within the brain. This is in contradistinction to ionizing radiation used in external beam radiation therapy, in which high-energy beams at the higher frequency end of the electromagnetic spectrum are delivered to tissues, which are amenable to dosimetry delineation of the tumor target. In both cases significant computer resources are required for treatment planning and verification. While in external beam radiation therapy the challenge is represented by difficulties in determining the tissue cross sections and the presence of heterogeneous geometries, leading to complex radiation transport simulations based on a priori diagnostic imaging information, the nature of the problem in TTFields therapy is different. Instead of

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having to solve the coupled charged particle-photon linear Boltzmann equation, solutions to the coupled Maxwell equations are needed to visualize directly how TTFields infiltrate the tumor and the surrounding brain tissues. The methods of computation, such as finite element analysis, and root-finding algorithms (e.g., Newton-Raphson method), rely on computer software like Mimics® (Materialize, Belgium) or ScanIP® (Simpleware, UK) and COMSOL Multiphysics® (COMSOL Burlington, Massachusetts, USA) for imaging processing and simulation.

Energy Delivery via Tumor Treating Fields Versus Ionizing Radiation

TTFields and ionizing radiation deliver energies using significantly different parts of the electromagnetic spectrum. The frequency at which TTFields operate is in the kilohertz or 10^3 cycles/seconds range with a wavelength of about ten football fields long, and the amount of energy delivered is quantified in terms of power per unit mass (W/kg) or energy per unit time per unit mass (J/s/kg), which is the dose rate. In contrast, X-rays and gamma rays operate in the exahertz or 10^{16} cycles/seconds range with a wavelength smaller than the diameter of a hydrogen atom, and the energy delivered over a specific time interval is measured in terms of the dose with units of J/kg or Gy. While most external beam radiation therapy uses ionizing radiation with beam-on time of only a few minutes per fraction, the duration of TTFields therapy is orders of magnitude longer. Therefore, on a per unit time basis, TTFields deliver a lower amount of energy to the target tissue than ionizing radiation. Nevertheless, they both damage actively dividing tumor cells and effect downstream anticancer responses. Apart from this similarity, the two types of therapies diverge in their mechanisms of action.

According to the current theory of radiobiology, irreparable radiation injury of cells leads to mitotic death. Therefore, ionizing radiation damages tumors more effectively than normal tissues because tumor cells actively divide and undergo the mitotic process more often than normal cells. There are two main mechanisms of damage, direct and indirect actions, which form the basis for ionizing radiation's anticancer efficacy. In the case of direct action the incident radiation directly ionizes subcellular targets like DNA causing breaks in chemical bonds, which in turn can lead to single- and double-strand DNA breaks (SSB and DSB) resulting in cell death if not repaired [1–4]. Indirect action is mediated by reactive molecular species such as solvated electrons and free radicals, which are generated via the radiolysis of water. They can also cause SSB and DSB in the DNA and other types of damage to cellular organelles within the tumor [5, 6]. Unfortunately, the effects of radiation cannot be confined to the tumor, and limited damage to adjacent normal tissue is almost inevitable despite the ever-increasing sophistication of treatment planning and delivery. Therefore, radiation necrosis, radiation-induced encephalopathy, and radiation-induced myelopathy are some of the consequences of ionizing radiation's side effects in the central nervous system [7–9].

TTFields deliver energy into a given mass of tissue continuously and the alternating electric fields target specifically those subcellular components of the mitotic machinery that have high dipole moments. Two such components, namely α/β tubulin and septin that have respective dipole moments of 1660 and 2711 Debyes [10], have been observed to be disrupted by TTFields during the transition from metaphase to anaphase in dividing tumor cells, leading to downstream interference with chromosome segregation and cytokinesis [11, 12]. The treated tumor cells may not die immediately but may need to go through multiple rounds of division before they die of apoptosis or immunogenic cell death [13, 14]. However, no toxicities within the brain have been observed and the major adverse events appear to be dermatological in nature, manifesting as scalp irritation [15].

Computational Physics and Simulation

Current methods of computational physics rely on a combination of (1) comprehensive understanding of the problem to be solved and the development of its mathematical model, (2) appropriate analytical and numerical methods and their combinations that implement an efficient approach to solving these problems, and (3) available computational hardware to perform the simulations. In an idealized situation, many physical behaviors can be modeled by the application of the fundamental laws of physics, alone or in combinations, and their solutions obtained analytically. However, in practice, most problems are too complex to be solved analytically and approximations are necessary both in the mathematical model and its solution. One of the methods in solving boundary value problems in partial differential equations, which is often used in TTFields modeling, is the finite element method (FEM). Early applications of FEM were first introduced in mechanical engineering, most notably in fluid dynamics by the aerospace industry during the 1950s and 1960s [16–19]. With the advent of faster digital computers, it has recently gained wide acceptance in other fields as well.

To visualize the electric field distribution within the brain delivered by the Optune® device, the computational procedures involve three essential steps: (1) segmenting various brain structures, (2) applying appropriate conditions and material properties, and (3) solving the coupled Maxwell equations using finite element analysis. First, patient image datasets, including MRI (T1, T2, and MP RAGE), CT, and PET, are typically acquired as DICOM formatted image files, which are then co-registered using post-acquisition processing software such as Mimics® or ScanIP®. Co-registration of various scanning techniques is essential in order to produce segmented structures of the various types of tissues and cavities within the brain, allowing for optimal visualization and high fidelity in processing anatomic structures that have low contrast (Fig. 4.1). For example, it is rather difficult to discern between white matter and gray matter in the brain on CT but they can be distinguished easier on MRI. Likewise, lymph nodes in the body that are infiltrated by tumors are much harder to detect on CT scans but are readily identified on PET due to the uptake of ¹⁸fluorodeoxyglucose by

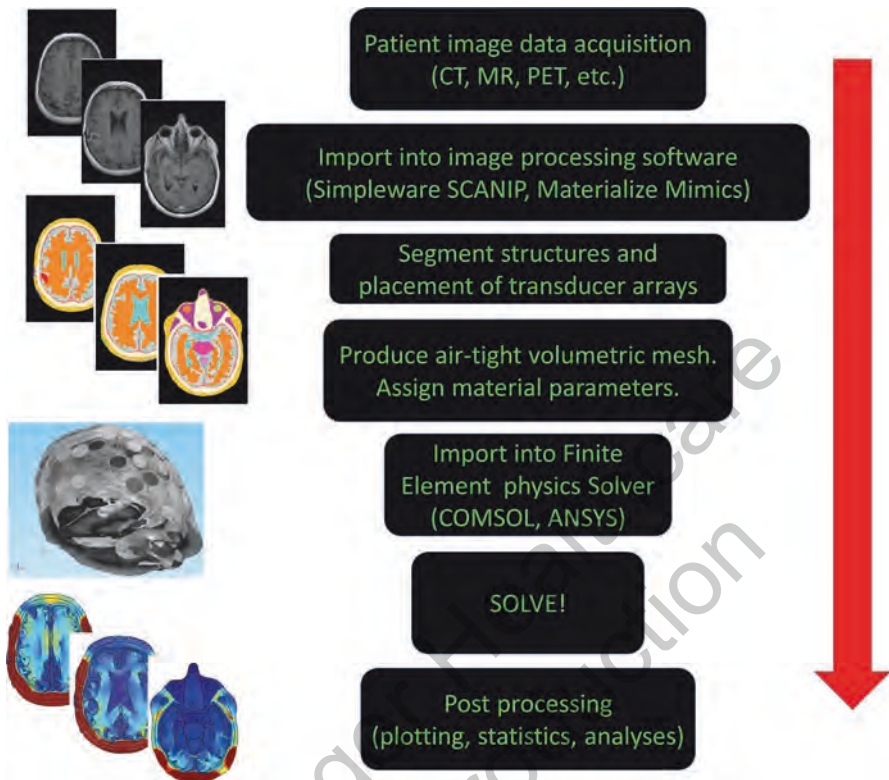


Fig. 4.1 Workflow diagram for segmentation, co-registration, and computer simulation of electric field distribution within the brain

tumor cells. From these co-registered images, the main anatomic structures are segmented into separate masks. When all the structures have been completely segmented, including filling in “islands” and small cavities by a combination of manual and automated segmentation techniques, a completely filled 3-dimensional mesh is then generated based on the segmented volumes. This 3-dimensional mesh (Fig. 4.2) is then imported into a finite element solver such as the one from COMSOL Multiphysics® to solve the coupled Maxwell equations and produce a visualization of the electric field distribution in the human brain.

Although segmentation of various tissues and structures can be completed using a combination of automated features available in the image post-processing software, the results do not always turn out to be accurate or produced with high fidelity. As suggested in a study by Guo D. et al. [20], the digitized results from automated segmentation by statistical parametric mapping produce pixels in the FEM that do not optimally represent the true geometry and in the numerical solution of Maxwell’s equations result in errors or singularities due to poor convergence. These non-convergent pixels (a.k.a. “dead” or “floating” pixels) require manual correction [20].

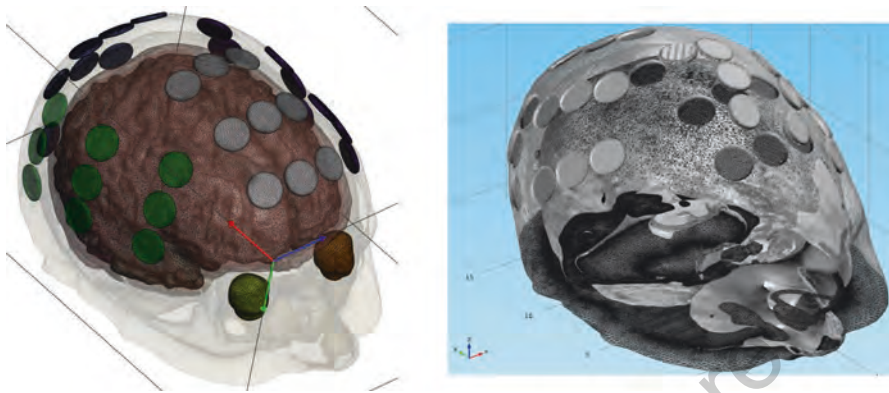


Fig. 4.2 A 3-dimensional representation of human head generated based on segmented volumes before (left) and after (right) importation into a finite element solver

Although the presence of several non-convergent pixels may not necessarily change the computation of the electric field distribution in a significant way, one must strive to eliminate these errors in order to obtain the best possible representation. However, an even more important reason to eliminate the floating pixels is to reduce the chance of producing a singularity in the result due to the inability to produce a correct finite element representation of the geometry over the affected pixel, or producing a singularity-like result due to dramatic changes in physical parameters such as electric conductivity. Therefore, it is imperative not to disregard such errors while preparing the finite element mesh.

When the mesh has been imported into a finite element solver, physical parameters that represent the composition of the various segmented anatomical structures are applied to each structure along with initial and boundary conditions as well as input parameters for the computation. For instance, in order to solve for the electric field distribution throughout the brain from TTFields induced by the transducer arrays that are placed against the scalp as seen in Fig. 4.3, the electric conductivity and relative permittivity values are applied to each segmented volume in the mesh model. Initial conditions for these domains include an assumed initial electric potential=0 or current density=0, and the boundaries between all domains and elements are continuous. Input parameters may include the applied voltage or current from the transducer arrays following a standard sinusoidal waveform as described in Chapter 2.

Newton-Raphson Method for Iterative Root Finding

The distribution of TTFields cannot be solved analytically and therefore numerical techniques must be used to approximate the solution. One of the most basic techniques of numerically finding the roots of a set of coupled equations that otherwise

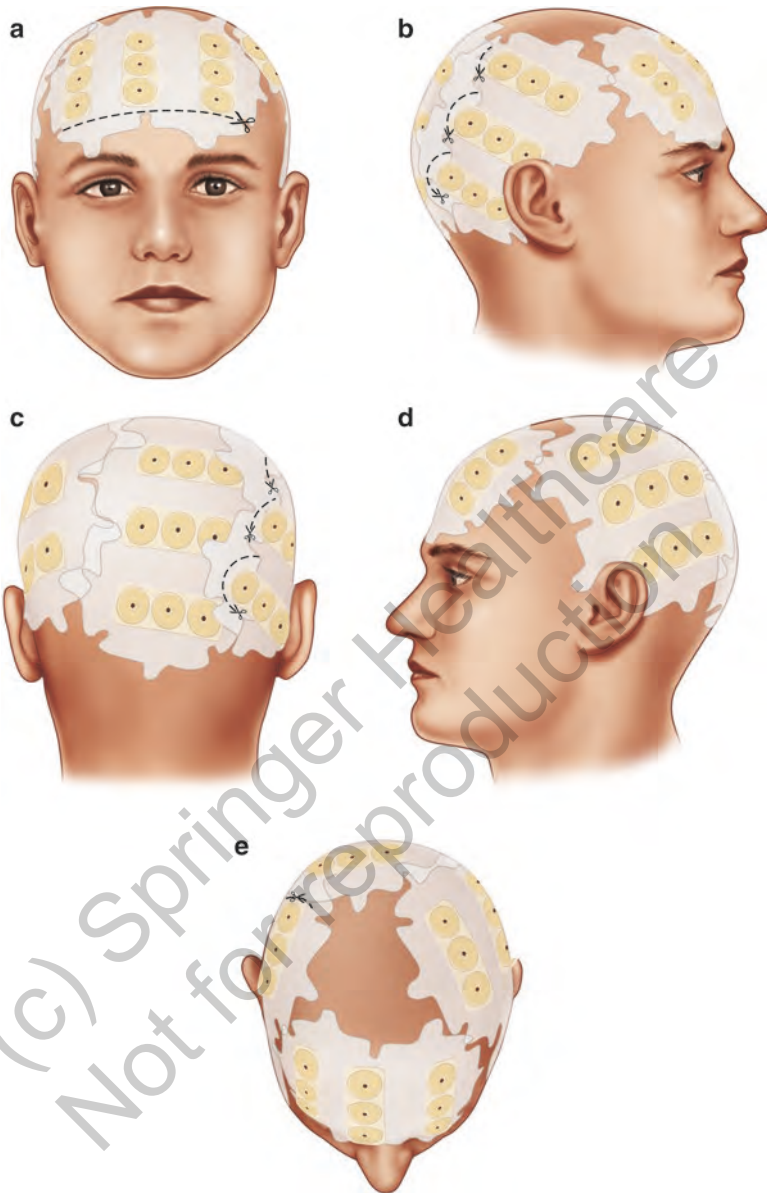


Fig. 4.3 NovoTAL™ transducer array mapping diagram. Four transducer arrays are arranged orthogonally on the surface of the shaved scalp as seen, from the right-to-left direction, at the (a) anterior, (b) right, (c) posterior, (d) left, and (e) top configurations

cannot be solved analytically is the Newton-Raphson method [21]. This method is an iterative procedure that minimizes the error each time an approximate solution is computed. Many finite element solvers use an adaptation of the Newton-Raphson method to solve a large number of simultaneous equations by way of organizing them into matrices consisting of many elements. The following is an example of using the Newton-Raphson method to iteratively solve three coupled equations in a 3×3 matrix.

Consider the system of equations written as a vector space of functions:

$$\bar{f}(\bar{T}) = 0, \quad \text{where } \bar{T} = (x, y, z) \therefore \bar{f}(x, y, z) = \begin{bmatrix} x^2 + 2y^2 + 3z^2 - 3 \\ 2x^2 + 5y^2 - z - 1 \\ x + 4y + z - 7 \end{bmatrix}$$

with an initial guess $\bar{T}^{(0)} = (x^{(0)}, y^{(0)}, z^{(0)}) = (1, 0, 1)$.

The Jacobian of $\bar{f}(x, y, z)$ is

$$J_f(x, y, z) = \nabla \cdot \bar{f} = \begin{bmatrix} \frac{\partial f_1}{\partial x} & \frac{\partial f_1}{\partial y} & \frac{\partial f_1}{\partial z} \\ \frac{\partial f_2}{\partial x} & \frac{\partial f_2}{\partial y} & \frac{\partial f_2}{\partial z} \\ \frac{\partial f_3}{\partial x} & \frac{\partial f_3}{\partial y} & \frac{\partial f_3}{\partial z} \end{bmatrix} = \begin{bmatrix} 2x & 4y & 6z \\ 4x & 10y & -1 \\ 1 & 4 & 1 \end{bmatrix}.$$

Solving the relationship $J_f(x^{(k)}, y^{(k)}, z^{(k)}) (\bar{T}^{(k+1)} - \bar{T}^{(k)}) = -\bar{f}(x^{(k)}, y^{(k)}, z^{(k)})$, where k is the iteration step, requires setting up the problem of interest and substituting the initial guess $\bar{T}^{(0)}$:

$$\begin{bmatrix} 2x & 4y & 6z \\ 4x & 10y & -1 \\ 1 & 4 & 1 \end{bmatrix} \begin{bmatrix} x^{(k+1)} - x^{(k)} \\ y^{(k+1)} - y^{(k)} \\ z^{(k+1)} - z^{(k)} \end{bmatrix} = - \begin{bmatrix} (x^{(k)})^2 + 2(y^{(k)})^2 + 3(z^{(k)})^2 - 3 \\ 2(x^{(k)})^2 + 5(y^{(k)})^2 - z^{(k)} - 1 \\ x^{(k)} + 4y^{(k)} + z^{(k)} - 7 \end{bmatrix}$$

$$\begin{bmatrix} 2(1) & 4(0) & 6(1) \\ 4(1) & 10(0) & -1 \\ 1 & 4 & 1 \end{bmatrix} \begin{bmatrix} x^{(0+1)} - 1 \\ y^{(0+1)} - 0 \\ z^{(0+1)} - 1 \end{bmatrix} = - \begin{bmatrix} 1 \\ 0 \\ -5 \end{bmatrix}$$

$$\begin{bmatrix} 2 & 0 & 6 \\ 4 & 0 & -1 \\ 1 & 4 & 1 \end{bmatrix} \begin{bmatrix} x^{(1)} - 1 \\ y^{(1)} - 0 \\ z^{(1)} - 1 \end{bmatrix} = - \begin{bmatrix} 1 \\ 0 \\ -5 \end{bmatrix}$$

$$\begin{bmatrix} 2x + 0y + 6z \\ 4x + 0y - z \\ x + 4y + z \end{bmatrix} = \begin{bmatrix} 7 \\ 3 \\ 7 \end{bmatrix}$$

Now, the first iterative solution $\bar{T}^{(1)}(x^{(1)}, y^{(1)}, z^{(1)})$ consists of:

$$\begin{bmatrix} 2 & 0 & 6 \\ 4 & 0 & -1 \\ 1 & 4 & 1 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 7 \\ 3 \\ 7 \end{bmatrix}.$$

At this point, this is similar to a classic linear algebra problem:

$$A^{-1}AX = A^{-1}B$$

$$A^{-1}A = I, \quad \text{where } I \text{ is the identity matrix } I = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}, \quad \text{so that } IX = X$$

$$\therefore X = A^{-1}B.$$

In order to determine the inverse of matrix A , the following definition is used:

$$A^{-1} = \frac{1}{\det(A)} \text{adj}(A)$$

For a matrix $A = \begin{bmatrix} a & b & c \\ d & e & f \\ g & h & i \end{bmatrix}$, $\det(A) = a \begin{bmatrix} e & f \\ h & i \end{bmatrix} - b \begin{bmatrix} d & f \\ g & i \end{bmatrix} + c \begin{bmatrix} d & e \\ g & h \end{bmatrix}$

$$\det \begin{bmatrix} 2 & 0 & 6 \\ 4 & 0 & -1 \\ 1 & 4 & 1 \end{bmatrix} = 2 \begin{bmatrix} 0 & -1 \\ 4 & 1 \end{bmatrix} - 0 \begin{bmatrix} 4 & -1 \\ 1 & 1 \end{bmatrix} + 6 \begin{bmatrix} 4 & 0 \\ 1 & 4 \end{bmatrix}$$

$$\det(A) = 2[(0 \cdot 1) - (-1 \cdot 4)] - 0[(4 \cdot 1) - (1 \cdot -1)] + 6[(4 \cdot 4) - (1 \cdot 0)] = 104$$

Now, $\text{adj } A = \text{Cofactor Matrix}^T$; where T indicates the transpose operation.

$$\begin{aligned}
\text{Cofactor}(A) &= \begin{bmatrix} + & - & + \\ - & + & - \\ + & - & + \end{bmatrix} \begin{bmatrix} A_{11} & A_{12} & A_{13} \\ A_{21} & A_{22} & A_{23} \\ A_{31} & A_{32} & A_{33} \end{bmatrix} \\
&= \begin{bmatrix} + & - & + \\ - & + & - \\ + & - & + \end{bmatrix} \begin{bmatrix} \begin{vmatrix} 0 & -1 \\ 4 & 1 \end{vmatrix} & \begin{vmatrix} 4 & -1 \\ 1 & 1 \end{vmatrix} & \begin{vmatrix} 4 & 0 \\ 1 & 4 \end{vmatrix} \\ \begin{vmatrix} 0 & 6 \\ 4 & 1 \end{vmatrix} & \begin{vmatrix} 2 & 6 \\ 1 & 1 \end{vmatrix} & \begin{vmatrix} 2 & 0 \\ 1 & 4 \end{vmatrix} \\ \begin{vmatrix} 0 & 6 \\ 0 & -1 \end{vmatrix} & \begin{vmatrix} 2 & 6 \\ 4 & -1 \end{vmatrix} & \begin{vmatrix} 2 & 0 \\ 4 & 0 \end{vmatrix} \end{bmatrix} \\
&= \begin{bmatrix} + & - & + \\ - & + & - \\ + & - & + \end{bmatrix} \begin{bmatrix} 4 & 5 & 16 \\ -24 & -4 & 8 \\ 0 & -26 & 0 \end{bmatrix} \\
&= \begin{bmatrix} 4 & -5 & 16 \\ 24 & -4 & -8 \\ 0 & 26 & 0 \end{bmatrix}
\end{aligned}$$

To find the transpose of this cofactor matrix, we have

$$\begin{bmatrix} 4 & -5 & 16 \\ 24 & -4 & -8 \\ 0 & 26 & 0 \end{bmatrix}^T = \begin{bmatrix} 4 & 24 & 0 \\ -5 & -4 & 26 \\ 16 & -8 & 0 \end{bmatrix}.$$

We then compute $A^{-1} = \frac{1}{\det(A)} \text{adj}(A)$:

$$A^{-1} = \frac{1}{104} \begin{bmatrix} 4 & 24 & 0 \\ -5 & -4 & 26 \\ 16 & -8 & 0 \end{bmatrix} = \begin{bmatrix} \frac{4}{104} & \frac{24}{104} & 0 \\ -\frac{5}{104} & -\frac{4}{104} & \frac{26}{104} \\ \frac{16}{104} & -\frac{8}{104} & 0 \end{bmatrix} = \begin{bmatrix} \frac{1}{26} & \frac{3}{13} & 0 \\ -\frac{5}{104} & -\frac{1}{26} & \frac{1}{4} \\ \frac{2}{13} & -\frac{1}{13} & 0 \end{bmatrix}$$

Finally, returning to the original problem,

$$X = A^{-1}B = \begin{bmatrix} \frac{1}{26} & \frac{3}{13} & 0 \\ -\frac{5}{104} & -\frac{1}{26} & \frac{1}{4} \\ \frac{2}{13} & -\frac{1}{13} & 0 \end{bmatrix} \begin{bmatrix} 7 \\ 3 \\ 7 \end{bmatrix} = \begin{bmatrix} x = \frac{25}{26} \\ y = \frac{135}{104} \\ z = \frac{11}{13} \end{bmatrix} = \bar{T}^{(1)}(x^{(1)}, y^{(1)}, z^{(1)})$$

In order to find an acceptable solution, we repeat the procedure using $\bar{T}^{(k)}$ as the next “guess” until $\bar{T}^{(k+1)}(x^{(k+1)}, y^{(k+1)}, z^{(k+1)})$ converges to the same vector $\bar{T}^{(k)}$, or until a desired error tolerance is met. Proof of this concept may be confirmed by computing more iterations as an exercise.

Solving for the Electric Field Distribution in the Human Head

Though it may be tempting to think that in complex geometry, FEM is the key to solving most applied mathematical problems involving partial differential equations and boundary conditions, such as Maxwell’s equations. However, the accuracy of FEM is limited by a number of factors, including the element size, the input parameters, computer hardware and kernel efficiency that represents smoothing of random fluctuations in the iterative solution. As multiple research groups have attempted to solve for the electric field distribution in the human head using FEM, the preparative technique is relatively standardized and involves the use of MR images of a human head for (1) segmentation of various tissue structures, (2) generation of a 3-dimensional mesh for each segmented volume, and (3) importation of the composite mesh into a finite element solver [22–27]. Likewise, the approach to solving for the electric fields is also relatively standardized. This involves (1) identifying and applying physical parameters to different segmented tissue types, (2) specifying appropriate boundary and initial conditions, and (3) solving for the distribution of electric fields, all of which are dependent on the transducer array layout.

Transducer Array Layout for the Delivery of Tumor Treating Fields

TTFields are delivered via two pairs of transducer arrays placed orthogonally on the shaved surface of the scalp. They are arranged in an anterior-posterior and right-left orientation (Fig. 4.3). Each array has nine circular ceramic disks with a diameter of 2.0 cm and spaced 0.5 cm apart along the short axis and 0.7 cm apart along the long axis. The surface of each ceramic disk has a thin layer of conductive gel that provides good conductivity [28], while nine disks positioned as a 3×3 array are secured on the scalp by a larger piece of insulated adhesive tape measuring $14.5 \text{ cm} \times 10.0 \text{ cm}$ [29]. TTFields are generated by a battery-powered alternating current generator, operating at 200 kHz with maximum voltage alternating from +50 to −50 V. This generator can be connected to a power cord that is plugged into a regular electric outlet when patients are stationary in bed or chair. It can also be connected to a portable lithium ion battery pack, both of which can be carried by ambulatory patients in a backpack. This portable system currently weighs 7 lb but newer generation of this device will weigh substantially less. The portable battery pack can be



Fig. 4.4 Overview of the components of the Optune® device as described in the U.S. Food and Drug Administration labeling (http://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034c.pdf)

recharged in a battery charger unit that can simultaneously charge four battery packs and it takes about 6 hours for the battery packs to be fully charged. The components of the Optune® device system are outlined in the U.S. Food and Drug Administration labeling of this device (Fig. 4.4) [29].

The transducer arrays are placed onto patients as shown in Fig. 4.3 according to a placement map generated by proprietary computer software called NovoTAL™ from Novocure. This map is generated based on the head dimensions (anterior-to-posterior, right-to-left, and right-to-midline) and dimensions of a tumor justified to the right border of the head by convention. These measurements submitted into the NovoTAL™ software program allow for the generation of a transducer array placement map. Although the exact method of generating this placement map is not disclosed, it is most likely built on known methods of electrode placement for

transcranial direct or alternating current stimulation. Electrode placement for transcranial current stimulation is done by using known conductivity values of the tissues in the head and brain, as well as the conductivity property of the ceramic disk used. Using FEM, the distribution of the electric fields can be estimated by setting the appropriate boundary conditions and material properties, and solving the coupled time-varying Maxwell's equations as explained in Chapter 2 [30]. Various mathematical algorithms such as inverse treatment planning and Monte Carlo simulation can be applied to generate, via an iterative process, the best fit positioning of the arrays [30–32]. Once penetrated into the head, these electric fields are most likely to be distorted by the electric properties of various intracranial structures based on each structure's conductivity and relative permittivity.

General Procedure for Treatment with Tumor Treating Fields

The U.S. Food and Drug Administration's approval of the Optune[®] device is currently for patients with recurrent and newly diagnosed glioblastoma. Since the device is self-contained and portable, in practice the patient is undergoing treatment as long as the transducer arrays are continuously in contact with the scalp as directed and powered by the TTFields generator. The positioning of the transducer arrays is currently dictated by NovoTAL[™], the array-positioning software provided to the physicians by Novocure, whereas the positioning of the arrays is based on the tumor dimensions as seen on MRI. There is no other treatment planning protocol currently being used for clinical purposes. Once the treating physician or physician assistant reviews the placement procedures and compliance requirements with the patient after informed consent, the arrays are placed onto the scalp and the patient is sent home with the portable battery pack and generator, which are fitted into a small shoulder bag.

Conclusions

TTFields therapy exerts its anticancer effect by disrupting tumor cell division during metaphase-to-anaphase transition in mitosis. The fields are targeted against α/β tubulin and septin that have large dipole moments, which are necessary for proper cellular division. The visualization of the electric field distribution requires computer modeling that takes into account several intracranial tissue parameters such as spatially varying conductivity and relative permittivity. This is done by segmenting various tissue structures, generating a 3-dimensional mesh for each segmented volume, and importing the composite mesh into a finite element solver, which requires (1) the identification and application of physical parameters to different segmented tissue types, (2) specification of appropriate boundary and initial conditions, and (3)

identification of the best solution for the electric field distribution, all of which are dependent on the transducer array layout.

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Chapter 5

Response Pattern and Modeling of Tumor Treating Fields

Josef Vymazal, Aaron M. Rulseh, and Eric T. Wong

Glioblastoma multiforme (GBM) is the most common primary malignant brain tumor [1, 2], with a global incidence of approximately 3.5 per 100,000 people [2]. Despite standard treatment consisting of surgical resection together with radiotherapy and concomitant/adjuvant temozolomide chemotherapy, the median overall survival (OS) for patients with newly diagnosed GBM is only 12 to 18 months [1–3]. Nearly all patients with GBM experience disease progression despite aggressive first-line therapy, with a median time to progression of 6 to 11 months [1, 4]. Treatment options for GBM at the time of recurrence are limited, and there is no widely accepted standard treatment [4–6]. Thus, new and more effective treatment options are highly desirable.

The Optune® device (Novocure Ltd., Haifa, Israel) is an approved antimitotic treatment for patients with recurrent or newly diagnosed GBM [6–8]. It delivers intermediate-frequency alternating electric fields at 200 kHz, also known as Tumor Treating Fields (TTFields), via noninvasive transducer arrays applied to the scalp based on computerized treatment planning according to anatomic magnetic resonance imaging (MRI) of the tumor [9]. TTFields selectively kill or arrest the

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growth of rapidly dividing cells by inhibiting the proper formation of the mitotic spindle and by causing rapid plasma membrane disruption during cytokinesis [10–13]. Therefore, this treatment is selective for dividing cells and requires continuous application for maximal benefit.

Response Pattern to Tumor Treating Fields

In GBM patients, response is usually characterized by at least a 50 % decrease in the product of the cross-sectional diameter of the tumor [14]. Although response is typically a secondary endpoint in GBM clinical trials, it usually signifies antitumor activity when present. In the initial pilot study of the Optune® device, ten subjects with recurrent GBM were treated with TTFields monotherapy after failing adjuvant temozolomide, while another ten with newly diagnosed GBM received TTFields plus maintenance temozolomide [15]. In the recurrent GBM cohort, there were two *bona fide* responses but their time to response was significantly delayed, with complete response realized in one subject at 6 months and partial response detected in another subject after 14 months [15]. Interestingly, in both tumors initial progression was detected on MRI 1 and 7 months after initiation of TTFields monotherapy. This initial worsening and subsequent shrinkage of the tumor on neuroimaging may be the result of an antitumor immune response as TTFields have been shown to evoke responses in tumor cells that are consistent with immunogenic cell death, including the cell surface expression of calreticulin and secretion of high-mobility group box 1 protein (HMGB1) [16]. Furthermore, TTFields-treated rabbits with implanted VX2 tumors in the sub-renal capsule had a reduced number of metastases to the lungs and these metastases had a significant increase in immune infiltrates [17].

In the phase III trial for recurrent GBM, 237 subjects were randomized in a 1:1 fashion to receive TTFields monotherapy ($n=120$) or best physician's choice chemotherapy ($n=117$) [6]. There were 14 responders, 3 complete and 11 partial responses, in the TTFields monotherapy cohort and 6 of them experienced initial tumor growth at an interval of 2 to 24 months while on treatment [6, 18]. The median time to response and the response duration in these patients were longer compared to those who received chemotherapy, 8.4 months versus 5.8 months and 7.3 months versus 5.6 months, respectively [18]. These findings suggest that responders to TTFields may require a longer time to response but, once initiated, they have a more durable response than those treated with chemotherapy. These findings in the phase III trial for recurrent GBM also provide support for an immune-mediated component in the mechanism for TTFields' anti-GBM efficacy.

By combining the participants from both trials for recurrent GBM, there were a total of 16 responders, 2 from the pilot study and 14 from the phase III registration trial [6, 15]. As shown in Fig. 5.1, the median time to objective radiographic response in the 16 responders was 5.2 months (95 % CI 3.2–7.6 months), the median response duration was 12.9 months, and the median overall survival was 26.5 months. Figures 5.2, 5.3, 5.4, and 5.5 show exemplary post-gadolinium-enhanced

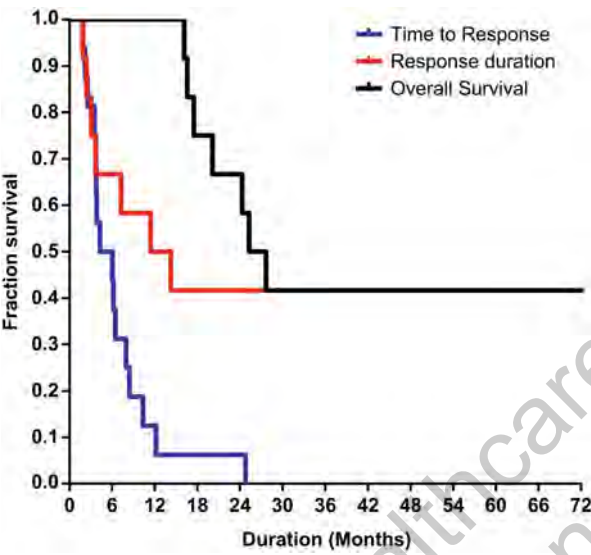


Fig. 5.1 Kaplan-Meier estimates of the time to radiological response according to Macdonald criteria (blue), response duration (red), and overall survival (black) of the 16 responders combined from the pilot study and the phase III trial for recurrent GBM [6, 15]. Vymazal et al. Response patterns of recurrent glioblastomas treated with tumor-treating fields. *Semin Oncol.* 41 Suppl 6:S14-S24, 2014. Elsevier

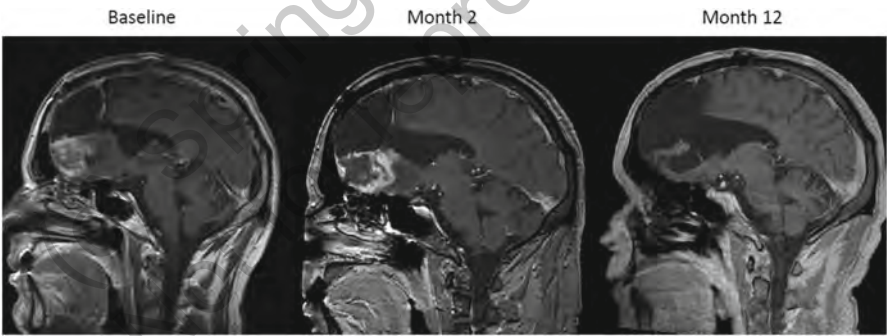


Fig. 5.2 T1-weighted post-contrast MR images of a 48-year-old man with prior grade II astrocytoma, which transformed to GBM as confirmed by tissue biopsy. The subject progressed after receiving radiotherapy with concomitant temozolomide followed by 3 cycles of adjuvant temozolomide. He subsequently responded to TTFields, achieved at 12 months, and remained stable for an additional 20 months while on treatment. Vymazal et al. Response patterns of recurrent glioblastomas treated with tumor-treating fields. *Semin Oncol.* 41 Suppl 6:S14-S24, 2014. Elsevier

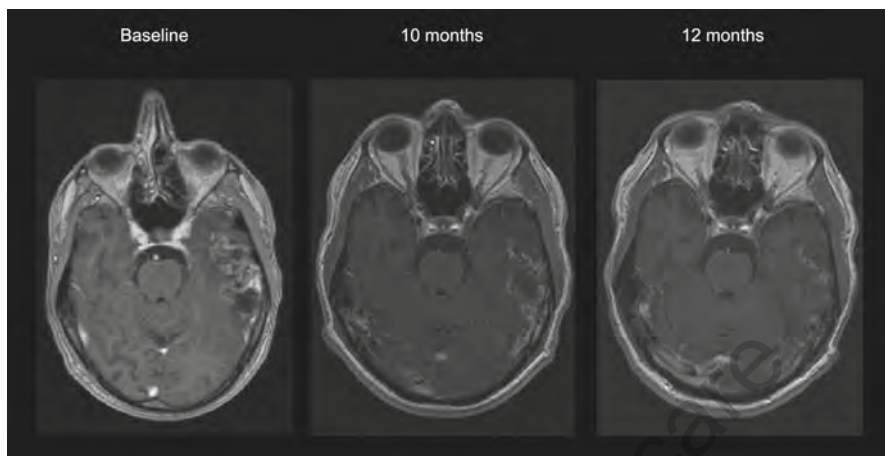


Fig. 5.3 T1-weighted post-contrast MR images of a 51-year-old man with primary GBM which recurred 6 months after chemoradiotherapy with temozolomide. The patient underwent a biopsy of the tumor only without surgical resection. He had a very gradual response, reaching a 50 % reduction in tumor size after 10 months on TTFields. He remained stable for an additional 2 months on treatment. Vymazal et al. Response patterns of recurrent glioblastomas treated with tumor-treating fields, *Semin Oncol.* 41 Suppl 6:S14-S24, 2014. Elsevier

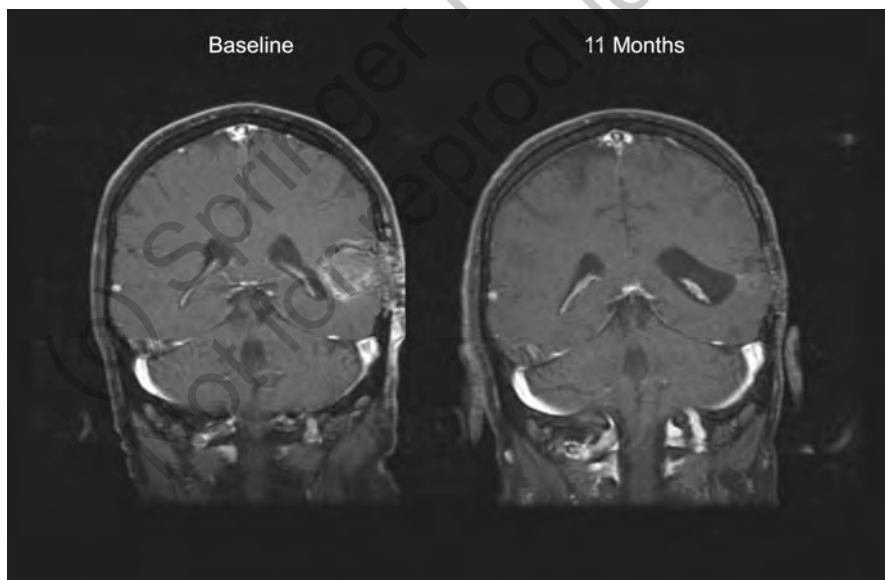


Fig. 5.4 T1-weighted post-contrast MR images of a 55-year-old man with primary GBM which recurred for the third time after receiving radiotherapy with concomitant temozolomide, 2 cycles of adjuvant temozolomide, 3 cycles of bevacizumab with irinotecan, and 1 cycle of erlotinib and sorafenib. The subject had a partial response after 4 months of treatment with TTFields and remained stable for an additional 8 months while on therapy. Vymazal et al. Response patterns of current glioblastomas treated with tumor-treating fields. *Semin Oncol.* 41 Suppl 6:S14-S24, 2014. Elsevier

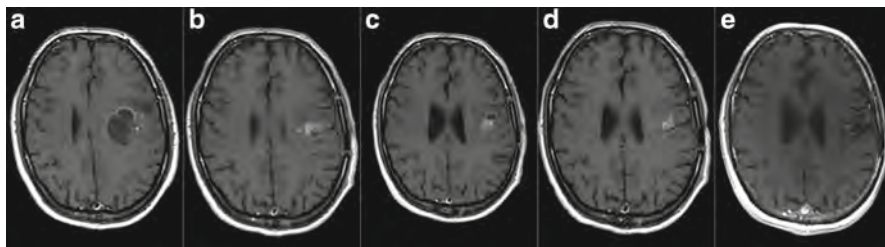


Fig. 5.5 T1-weighted post-contrast MR images of a 41-year-old man with GBM which recurred following partial surgical resection and radiotherapy with concomitant daily temozolomide. (a) Before initial surgery, GBM was detected on MRI in the left frontal region. (b) Seven months after initial diagnosis, an enhancing lesion suspected to be recurrent or residual tumor was detected and treatment with the Optune® device was initiated. (c) Seven months after initiation of TTFields, the enhancing lesion became partly cystic. (d) Ten months after initiation of TTFields, regression of the cystic portion of the lesion was detected, but a subtle enhancement was still present. (e) The faintly enhancing region remains without progression 94 months after initiation of TTFields. *GBM* glioblastoma multiforme, *MR* magnetic resonance, *TTFields* Tumor Treating Fields. Rulseh et al. Long-term survival of patients suffering from glioblastoma multiforme treated with tumor-treating fields. *World J Surg Oncol*. 10:220, 2012. BioMed Central

T1-weighted MR images of responders. The most important findings were that responses to TTField treatment developed relatively slowly and, in most cases, the responses were remarkably durable.

In 7 of the 16 responders (44%) from both studies, MRI showed initial tumor growth. Exemplary MR images of delayed responders can be found in Figs. 5.6 and 5.7. Median time to reversal of tumor growth in delayed responders was 4 (95 % CI 2.3–7.4) months. Initial tumor growth was accompanied by an increase in T2-weighted signal intensity in 5 of the 7 delayed responders (71 %) (Fig. 5.6). Diffusion-weighted imaging in 3 of the 7 delayed responders did not demonstrate increased signal in the first 4 months after treatment initiation. The averaged maximal tumor area over time compared to baseline in the delayed responders is shown in Fig. 5.8.

There was a correlation between response and prolonged survival in both cohorts in the trial, and responders treated with either TTFields monotherapy or chemotherapy lived longer than nonresponders. In the cohort treated with TTFields, the median overall survival was 24.8 months for responders and 6.2 for nonresponders, while it was 20.0 months for responders and 6.8 months for nonresponders in the cohort received chemotherapy [18]. Of note, a significant Pearson correlation was only found between time to response and overall survival, as well as between response duration and overall survival, in the TTFields cohort but not the chemotherapy cohort [18]. This suggests that a response in the TTFields-treated subjects predicts prolonged survival but this is not necessarily so for chemotherapy-treated subjects. In fact, 3 of the responders to TTFields in the phase III trial lived more than 40 months from the time of recurrence and 2 in pilot trial survived longer than 72 months from the time of treatment initiation [15, 18].

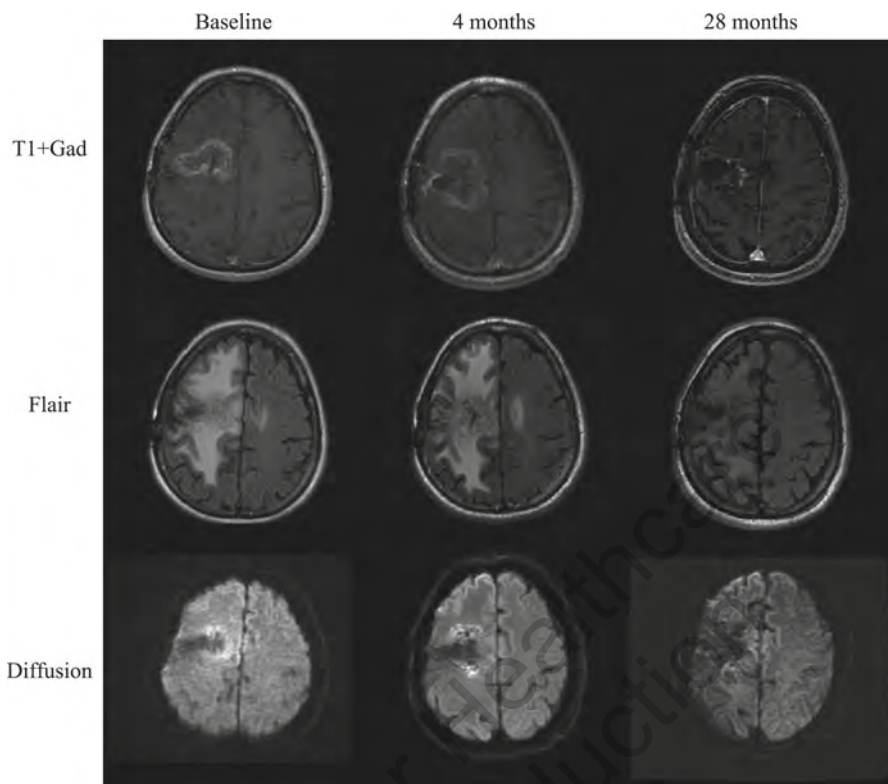


Fig. 5.6 T1-weighted post-contrast with corresponding FLAIR and diffusion MR images of a heavily pretreated 48-year-old man with secondary GBM. The patient underwent 3 debulking surgeries, radiotherapy with concomitant daily temozolomide, as well as Gamma knife boost. The tumor showed heterozygous deletions of 1p and 19q chromosomes and methylated *MGMT* promoter. The patient was treated with TTFields for 28 months until radiological response was achieved and has been on treatment for 45 months thus far. Notably, the tumor grew during the first 8 months on treatment and only then began to decrease in size. Additional MRI sequences show that the initial tumor growth was accompanied by increased FLAIR signal but not increased diffusion signal. Vymazal et al. Response patterns of recurrent glioblastomas treated with tumor-treating fields. *Semin Oncol.* 41 Suppl 6:S14-S24, 2014. Elsevier

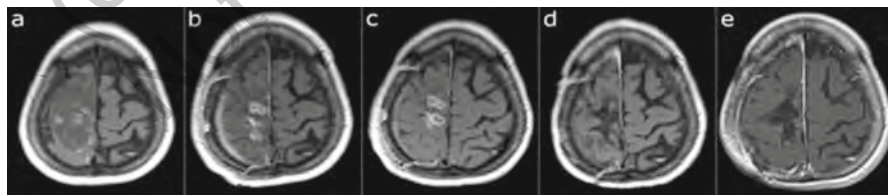


Fig. 5.7 T1-weighted post-contrast MR images of a 52-year-old woman with GBM, which recurred following surgical resection and radiotherapy with concomitant daily temozolomide. (a) GBM was identified in the right central region before initial surgery. (b) Three months following surgery and after radiotherapy with concomitant daily temozolomide, two enhancing lesions suspected to be recurrent tumor were detected. (c) One month after initiation of TTFields, the caudal enhancing lesion increased in size. (d) Six months after initiation of TTFields, both enhancing lesions regressed in size. (e) Both lesions underwent complete regression 8 months after initiation of TTFields and have remained so for another 117 months. Rulseh, et al. Long-term survival of patients suffering from glioblastoma multiforme treated with tumor-treating fields. *World J Surg Oncol.* 10:220, 2012. BioMed Central

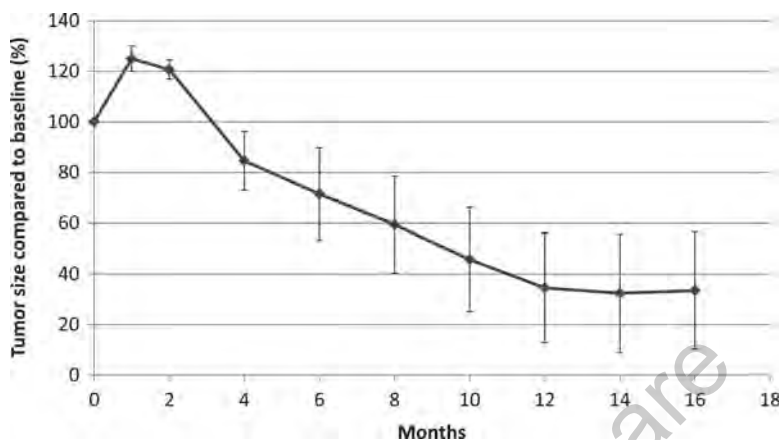


Fig. 5.8 Time course of normalized tumor size in the 7 delayed responders to TTFields. Data are presented as average tumor area \pm standard deviation normalized to baseline, or pretreatment, tumor area. Vymazal et al. Response Patterns of Current Glioblastomas Treated with Tumor-Treating Fields. *Semin Oncol.* 41:S14-S24. 2014. Elsevier

Predictive Factors for Response to Tumor Treating Fields

Despite responders to TTFields having similar baseline characteristics to the rest of the population in both trials [15, 18], there may be other factors correlated to radiological response, which continue to be the subject of active investigation. First, an increase in treatment compliance was associated with better response and longer overall survival [19]. This is most likely due to TTFields' mechanism of action, which only disrupts tumor cells during mitosis at the metaphase-to-anaphase transition, and as a result the Optune[®] device has to be applied continuously in order to exert benefit [12, 13]. Second, it has been suggested that tumor localization, as well as the internal composition of the tumor, may play a role in treatment response [20, 21]. As the ventricles have high water content and water acts as a conductor for electric fields, the mitotic disruption effect of TTFields may be maximized when the tumor is near the ventricular surface. Third, in the randomized phase III trial, patients with prior low-grade glioma histology, or secondary GBM, had a trend for increased median survival compared to those without [18]. This may be a result of slower rate of tumor growth among patients with secondary GBM [22] and therefore they may have more time for TTFields to exert its antitumor effect. Lastly, patients with GBM need dexamethasone to control neurologic symptoms and this corticosteroid in particular can lead to suppression of multiple immune effector systems that may be required for TTFields-induced tumor

rejection [23–25]. Specifically, a *post hoc* analysis of dexamethasone dosage taken by participants of the phase III trial using TTFields monotherapy or chemotherapy for recurrent GBM demonstrated that those who took <4.1 mg/day of dexamethasone lived significantly longer than those who received ≥ 4.1 mg/day [23]. Taken together, there may be multiple pathways to objective tumor response as a result of TTFields treatment, some of which are intrinsic while others are extrinsic to the patient's tumor.

Multi-Compartmental Model of Tumor Growth and Delayed Response

To better characterize tumor regression induced by TTFields, Vymazal and Wong [19] constructed a multi-compartmental kinetic model based on the states of cells within the tumor microenvironment, specifically between latency and replication as well as their progression to death and clearance. The model assumed that changes in tumor volume, for any given time interval, are determined by the number of cells in four dynamic compartments: (1) tumor cells in a dormant or latent (L) state, (2) cells that have left the dormant state to enter mitosis and replicate (R), (3) cells that have died (D) within the time interval, and (4) cells that have been cleared (C) from the tumor microenvironment (Fig. 5.9a). Dormant or latent (L) cells are in a reversible transition with the dividing or replicating (R) cells, with forward and reverse rate constants of k_1 and k_2 , respectively. The rate constants are balanced to keep the constituents of the two compartments at a fixed ratio consistent with the histologically determined fraction of dividing cells in GBM tumors. Tumor cells are assumed to die or move to the third compartment through two mechanisms. The first is apoptosis, which mainly depends on nutrient and oxygen supply (blood flow); to simplify the model, a single death rate constant, k_4 , was used. The second mechanism is the rate of replicating (R) cells progressing to death (D) due to TTFields, which is represented by the rate constant k_3 . The dead cells are removed from the vascularized layer of the tumor (at least in part via phagocytosis) by transferring them to a virtual fourth compartment with a rate constant k_5 (Fig. 5.9a). This model predicted, in GBM tumors continuously exposed to TTFields, a doubling of the baseline tumor volume at 4 weeks before a reduction in tumor volume near 7 months (Fig. 5.9b). This prediction is consistent with the observed tumor behavior, in which there was an initial increase in tumor size that constituted progressive disease, with tumor regression that qualifies as partial response occurring more than 8 months after the initiation of TTFields (Fig. 5.8). Therefore, we may expect that GBM tumors will cease to grow and start to regress in size only after several weeks of continuous exposure. However, objective tumor response may not occur until at least 5 to 8 months later.

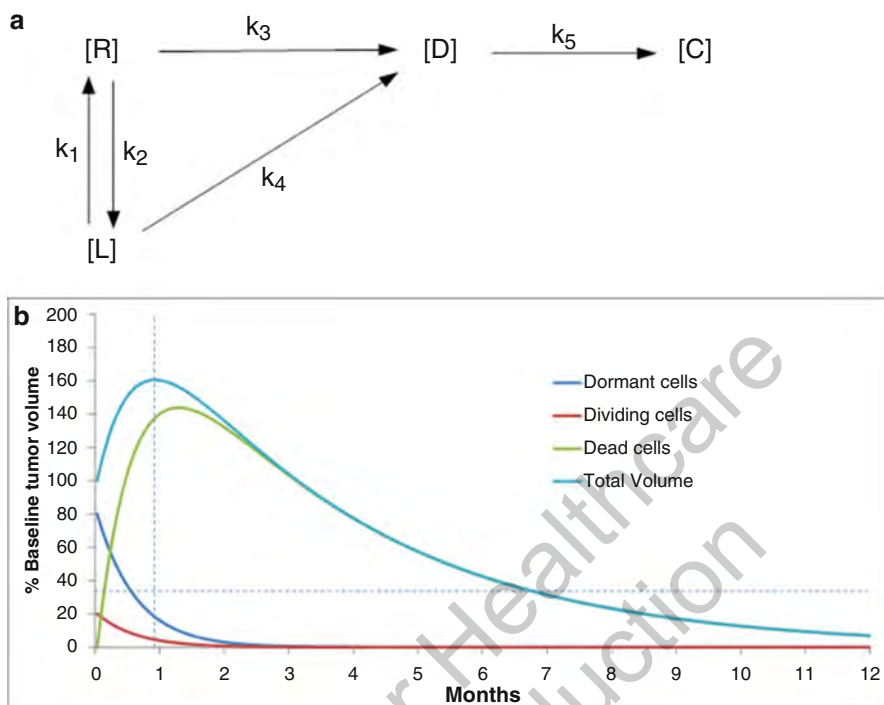


Fig. 5.9 Multi-compartmental kinetic model of tumor cells. **(a)** Schematic representation of the different compartments in the model and the rate constants associated with the interactions between them. TTFields were modeled as effecting k_3 . [L]=Latent/non-dividing cells; [R]=replicating/dividing cells; [D]=dead cells; [C]=cells cleared from tumor by physiological mechanisms. **(b)** Results of kinetic model simulation and relative changes in tumor compartment size. Volume changes during the initial 9 months of treatment with TTFields are characterized by growth of tumor volume in the initial month, with a maximum near 1 month followed by a gradual decline. A reduction of tumor volume to 35% is observed at about 6.8 months, equivalent to a 50% decrease in bi-dimensional tumor measurement or partial response according to the Macdonald or RANO criteria. Dormant cells (black); dividing cells (red); dead cells (green); total tumor volume (blue); vertical dashed line represents peak tumor volume and time of tumor growth reversal (28 days). Vymazal et al. Response patterns of recurrent glioblastomas treated with tumor-treating fields. *Semin Oncol.* 41 Suppl 6:S14-S24, 2014. Elsevier

Conclusion

In summary, TTFields represent a novel treatment option for patients with GBM. Among the trial participants with recurrent GBM, approximately 16 experienced a complete or partial radiological response that typically developed slowly, with a median time to response of 5.2 months, and was generally durable with a median duration of 12.9 months. Some of the responders have lived for 10 years or longer.

Seven of 16 (44%) GBM responders to TTFields exhibited radiological signs of tumor growth initially, before reversing and regressing in size after a median of 4 months, and a range of 2 to 7 months, of continuous treatment. Therefore, TTFields produce responses slowly and when tumor shrinkage occurs it is often durable. Furthermore, tumor response develops gradually and tumor growth may be observed initially even in eventual responders to this therapy. Thus, we recommend that TTFields should be continued for a sufficient amount of time and that initial radiologic progression following treatment initiation should not be considered a reason to discontinue treatment.

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Chapter 6

Clinical Efficacy of Tumor Treating Fields for Recurrent Glioblastoma

Eric T. Wong

Recurrent glioblastoma is typically identified based on an increase in size or presence of new tumor as seen on neuroimaging. In recurrent primary glioblastoma [1], the pathology is already established at initial diagnosis and, therefore, a neurosurgical procedure for the purpose of obtaining additional tissue solely for diagnosis is not necessary. However, in secondary glioblastoma, tissue confirmation is indicated when the prior diagnosis is a low-grade or anaplastic glioma [2]. If the patient previously had radiotherapy, confirming a glioblastoma diagnosis can be challenging because radiation-induced necrosis or hyalinized vasculature is not enough, while tumor-associated pseudopalisading necrosis or multicellular vascular hyperplasia is absolutely needed. Additionally, a definition of tumor growth has been established by the Macdonald criteria [3] and, more recently, by the Response Assessment in Neuro-Oncology (RANO) criteria [4]. Both use 2-dimensional measurement as defined by the product of the largest perpendicular diameters of the tumor on MRI. Although Macdonald criteria define enhancement on post-gadolinium T1-weighted image as the region of tumor, RANO differs in the definition of tumor by including provisions to account for a lack of enhancement when patients are on antiangiogenesis therapies [5] or, in cases of pseudoprogression, too much enhancement that occurs after radiation and concomitant temozolomide [6]. Despite these generally accepted criteria, invasion by microscopic tumor cells into the adjacent brain that cannot be readily detected on MRI is a major hallmark of progressing glioblastoma [7].

Survival is limited at the time of recurrence in glioblastoma patients and their ability to maintain tumor stability from treatment is compromised. Median overall survival (OS) is a dismal 25 weeks and median progression-free survival (PFS) is only 9 weeks [8]. A majority of patients are debilitated to such an extent that no

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further treatment would benefit them. For those who have preserved neurologic functions, typically defined as a Karnofsky performance status of 70 or better, aggressive treatments may preserve their neurological functions. Surgery's role is limited unless 90 % or more of the tumor can be removed safely to achieve a survival benefit [9], while carmustine-impregnated dissolvable polymer wafers, which are implanted into the cavity of the resected tumor, are the only intervention for recurrent glioblastoma that showed a slight survival advantage in a randomized phase III trial [10]. Radiosurgery can be performed on tumors that are small and well circumscribed, but this intervention is not believed to lengthen patient survival [11, 12]. Bevacizumab, a monoclonal antibody against vascular endothelial growth factor, is the most commonly used drug in this population [5]. Although it has a high radiographic response rate and can provide a period of neurologic stabilization and even improvement, bevacizumab also does not appear to make patients live longer [13, 14]. Therefore, new treatments are needed.

Tumor Treating Fields (TTFields) are another modality of anticancer treatment that use alternating electric fields at 200 kHz to disrupt tumor cell cytokinesis as they progress from metaphase to anaphase during mitosis [15, 16]. There are a number of downstream consequences, including (1) violent blebbing of the cytoplasmic membrane, (2) asymmetric chromosome segregation, (3) endoplasmic reticulum stress that leads to the upregulation of chaperonin such as calreticulin on the surface of cells, (4) immune recognition of disrupted cells, and (5) eventual immunogenic cell death mediated by either the innate or the adaptive immune system [16, 17]. The key proteins that trigger all these downstream effects are thought to be critical for mitosis, and they perform functions specific at the space and time domains near the end of metaphase and the beginning of anaphase. Furthermore, in order for such proteins to be influenced by TTFields at 200 kHz, they must possess a large dipole moment such that their disrupted functions will result in mitotic failure. Two such proteins, septin and tubulin, fit this profile and they have dipole moments of 2711 and 1660 Debyes [18]. Septin is a large heterotrimeric protein complex that helps organize the cytokinetic cleavage furrow in anaphase [19], while tubulin mediates the segregation of sister chromatids to the opposing centrioles [20]. Septin appears to have a stronger influence on this process because of its larger dipole moment and its disruption triggers violent cytoplasmic blebbing that may precede the segregation of sister chromatids. Furthermore, it is the mode of cell death mediated by the immune system, which is a consequence of the induction of cytoplasmic stress and the translocation of endoplasmic chaperonin to the tumor cell surface facilitating immune recognition, that is the critical process translatable into clinical efficacy [17].

Pilot Study of Tumor Treating Fields in Recurrent Glioblastoma

The first-in-human trial was a pilot study, conducted from 2004 to 2005, to evaluate the safety and efficacy of TTFields therapy in 10 patients with recurrent glioblastoma [21]. The most common adverse event was contact dermatitis that occurred in

the majority and was caused by hydrogel-induced irritation of the scalp. Two patients experienced tumor-related partial seizures. No hematologic or electrolyte toxicity was seen, except for elevated liver enzymes in those taking anticonvulsants. The median overall survival of the 10 patients was 14.4 months and the 1-year survival rate was 67.5 % [21]. The median time to tumor progression was 6.0 months [21]. There was one complete and one partial responder who were still alive, respectively, at 84 and 87 months from treatment initiation [22]. Furthermore, the intensity of electric fields as directly measured in another patient was validated to be within 10% of the values estimated by computer modeling, suggesting that TTFields applied on the scalp were able to penetrate into the intracranial compartments [21].

EF-11 was the First Randomized Trial Utilizing Tumor Treating Fields

The EF-11 phase III trial was conducted between 2006 and 2009 comparing TTFields monotherapy versus Best Physician’s Choice chemotherapy. The primary endpoint was OS and secondary endpoints included PFS, response rate, and quality of life assessment [23]. In the intent-to-treat population, the median OS was 6.6 months for TTFields compared to 6.0 months for chemotherapy, with a hazard ratio of 0.86 ($p=0.27$) (Fig. 6.1). About 31 % of the chemotherapy cohort received bevacizumab alone or in combination with chemotherapy. The median PFS of TTFields and chemotherapy was 2.2 months and 2.1 months, respectively, with a hazard ratio

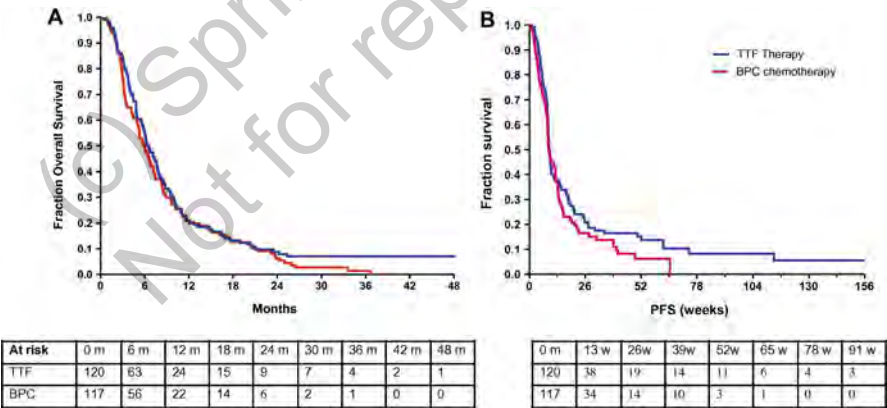


Fig. 6.1 Survival outcome in subjects enrolled in the EF-11 trial. Kaplan-Meier estimates of overall survival (A) and progression-free survival (B) in the TTFields monotherapy and Best Physician’s Choice chemotherapy cohorts in the EF-11 phase III trial. From Stupp et al. NovoTTF-100A versus physician’s choice chemotherapy in recurrent glioblastoma: A randomised phase III trial of a novel treatment modality. Eur J Cancer 48: 2192-2202, 2012. With permission from Elsevier

of 0.81 ($p=0.16$). In addition, the results demonstrated that the PFS at 6 months was 21.4 and 15.1 %, respectively ($p=0.13$). One-year survival rate was 20 % in both cohorts. The outcome of the trial indicates that TTFields have comparable efficacy when compared to chemotherapy and bevacizumab.

The most common adverse events associated with the device were grade 1 or 2 scalp irritation. Shifting of the arrays slightly during array change and applying topical corticosteroid can minimize this side effect [24]. There were far less hematological toxicities; other reported adverse events included appetite loss, constipation, diarrhea, fatigue, nausea, vomiting, and pain, which were associated with chemotherapy. Furthermore, additional analyses showed that device-treated patients had better cognitive and emotional functions. Based on the comparable efficacy results, superior safety profile, and a better quality of life, the U.S. Food and Drug Administration approved the Optune® device on April 8, 2011 for the treatment of recurrent glioblastoma.

Post Hoc Analysis of Prognostic Factors

The apparent discrepancy in the OS rates between the pilot study and the phase III trial prompted a series of *post hoc* analyses of the trial data. The first analysis centered on responders and it revealed two important characteristics. First, 5 of 14 responders treated with TTFields monotherapy had prior low-grade histology while none of the 7 responders treated with chemotherapy had that [25]. Second, the analysis revealed significantly less dexamethasone use in responders compared to nonresponders [25]. Responders in the TTFields monotherapy group received a median dexamethasone dose of 1.0 mg/day compared to nonresponders who received 5.2 mg/day ($p=0.0019$). Similar differences were also noted in the median cumulative dexamethasone dose of 7.1 mg for responders versus 261.7 mg for nonresponders ($p=0.0041$) (Fig. 6.2). In the chemotherapy cohort, the median dexamethasone dose used was 1.2 mg/day for responders versus 6.0 mg/day for nonresponders ($p<0.0001$). However, the median cumulative dexamethasone dose was not significantly different, 348.5 mg for responders versus 242.3 mg for nonresponders ($p=0.9520$) (Fig. 6.3). These data suggest that TTFields efficacy may be influenced by concurrent dexamethasone use, which is a clinically modifiable factor in the patient. This finding prompted an in-depth analysis of the dexamethasone effect in the entire trial population.

An unsupervised modified binary search algorithm was used to stratify the TTFields monotherapy arm of EF-11 based on the dexamethasone dosage that provided the greatest statistical difference in survival (Fig. 6.3). This analysis revealed that subjects who used >4.1 mg/day of dexamethasone had a markedly shortened median OS of 4.8 months as compared to those received ≤ 4.1 mg/day, who had a median OS of 11.0 months ($\chi^2=34.6$, $p<0.0001$) [26]. Subjects in the chemotherapy arm were observed to have a similar, but less robust, dichotomization and those who used >4.1 and ≤ 4.1 mg/day of dexamethasone had respective median OS of 6.0 and 8.9 months ($\chi^2=10.0$, $p=0.0015$). This difference in OS based on dexamethasone dose was unrelated to tumor size and most likely due to dexamethasone's interference with patient immune effector functions (Fig. 6.4). This notion was supported by

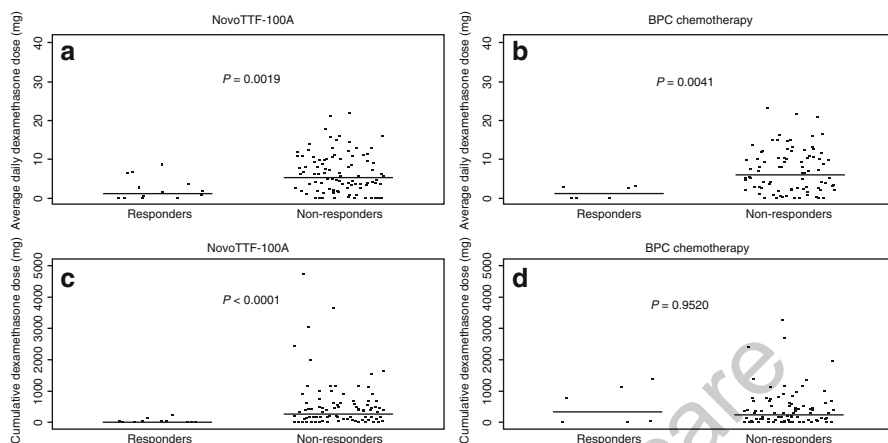


Fig. 6.2 Scatterplot of mean daily dexamethasone and cumulative dexamethasone dose in responders and nonresponders. (a) In the TTFields monotherapy cohort, the respective median and mean daily dexamethasone dose was 1.0 and 2.3 (95 % CI 0.8–3.8) mg for responders versus 5.2 and 6.8 (95 % CI 5.6–8.1) mg for nonresponders ($p=0.0019$). (b) In the BPC chemotherapy cohort, the respective median and mean daily dexamethasone dose was 1.2 and 1.4 (95 % CI 0.3–2.4) mg for responders versus 6.0 and 7.2 (95 % CI 6.0–8.4) mg for nonresponders ($p=0.0041$). (c) In the TTFields monotherapy cohort, the respective median and mean cumulative dexamethasone dose was 7.1 and 35.9 (95 % CI N/A to 72.5) mg for responders versus 261.7 and 485.6 (95 % CI 347.9–623.4) mg for nonresponders ($p<0.0001$). (d) In the BPC chemotherapy cohort, the respective median and mean cumulative dexamethasone dose was 348.5 and 525.6 (95 % CI 96.5–954.7) mg for responders versus 242.3 and 431.0 (95 % CI 328.1–533.8) mg for nonresponders ($p=0.9520$). *BPC* Best Physician’s Choice, *CI* confidence interval, *N/A* not available, *TTFields* Tumor Treating Fields. Wong et al. Response Assessment of versus best physician’s choice chemotherapy in recurrent glioblastoma. *Cancer Med.* 3(3): 592–602, 2014. John Wiley and Sons

a single-institution validation cohort of patients treated with TTFields, using their CD3⁺, CD4⁺, and CD8⁺ T lymphocytes as a marker of immune competency, and that showed their survival was impaired by a lower lymphocyte count suggesting immune competency is an important factor for TTFields efficacy (Fig. 6.4). In addition, a dexamethasone dosage of >4.0 mg/day, used by patients who were undergoing concomitant radiotherapy and daily temozolomide for their newly diagnosed glioblastoma, was also found to be a poor prognostic factor further supporting the conclusion that dexamethasone can impair the efficacy of treatment used in this population [27]. In both cohorts of the EF-11 trial, successive increases in dexamethasone usage above 4.1 mg/day were associated with progressive decrements in survival up to an inflection point near 8.0 mg/day, after which the rate of survival decreased slowly thereafter. Taken together, these data indicate that dexamethasone exerts a generalized and profound interference on the efficacy of both TTFields and chemotherapies against glioblastoma. Therefore, dexamethasone use should be aggressively minimized and other groups have since substantiated our finding [28, 29].

A re-analysis of the intent-to-treat population in EF-11 was performed to account for the insufficient treatment effect in 27 subjects who received less than 1 month or less than 1 cycle of TTFields monotherapy. This is because the antitumor effect of TTFields requires continuous administration, while chemotherapy can exert its effi-

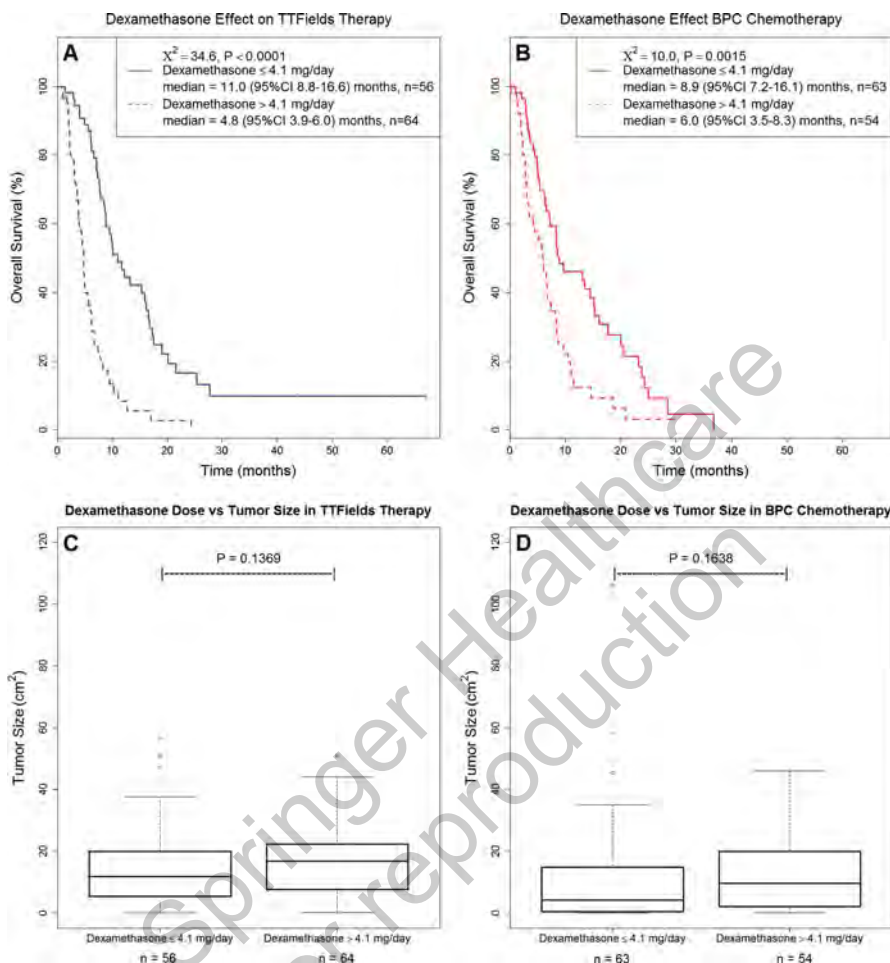


Fig. 6.3 Survival outcome stratified by dexamethasone dosage. Kaplan-Meier OS and tumor size with respect to dexamethasone requirement of ≤ 4.1 mg/day versus > 4.1 mg/day from subjects enrolled in the phase III trial comparing TTFields versus BPC chemotherapy. (A) Subjects enrolled in the TTFields treatment arm taking dexamethasone ≤ 4.1 (solid blue) mg/day versus > 4.1 (dashed blue) mg/day, which was determined by an unsupervised binary partitioning algorithm. Subjects who used ≤ 4.1 mg/day of dexamethasone ($n=56$) had a median OS of 11.0 months (95% CI: 8.8–16.6) as compared with those who used > 4.1 mg/day ($n=64$) with a median OS of 4.8 months (95% CI: 3.9–6.0) ($\chi^2=34.6, p<0.0001$). (B) Subjects enrolled in the BPC chemotherapy arm taking dexamethasone ≤ 4.1 (solid red) mg/day versus > 4.1 (dashed red) mg/day was determined by the same unsupervised binary partitioning algorithm. Subjects who used ≤ 4.1 mg/day of dexamethasone ($n=63$) had a median OS of 8.9 months (95% CI 7.2–16.1) as compared with those who used > 4.1 mg/day ($n=54$) with a median OS of 6.0 months (95% CI 3.5–8.3) ($\chi^2=10.0, p=0.0015$). (C) Box-and-whisker plot of the bi-dimensional tumor size in the TTFields monotherapy cohort that received dexamethasone ≤ 4.1 mg/day versus > 4.1 mg/day. Subjects who took dexamethasone ≤ 4.1 mg/day ($n=56$) had a median tumor size of 11.9 (range 0.0–56.7) cm^2 as compared with those who used > 4.1 mg/day ($n=64$) with a median tumor size of 16.8 (range 0.3–51.0) cm^2 ($p=0.1369$). (D) Box-and-whisker plot of the bi-dimensional tumor size in the BPC

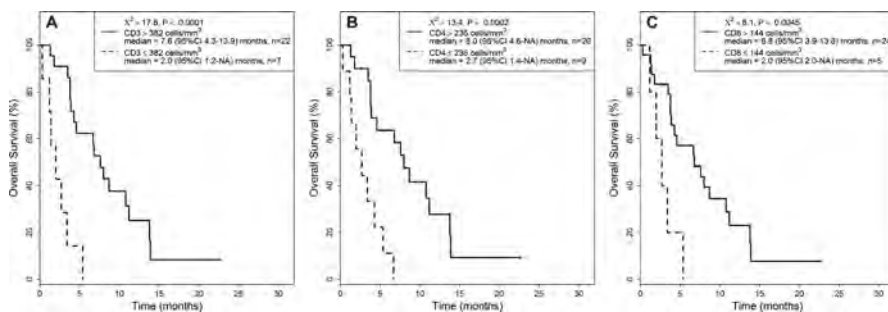


Fig. 6.4 Kaplan-Meier OS according to the optimal cutoff T-lymphocyte subsets as determined by an unsupervised binary partitioning algorithm. Confirmatory Wilcoxon's rank-sum test was also performed for (A) Median OS of patients with absolute CD3+ ≤382 cells/mm³ versus >382 cells/mm³ was 2.0 months (range 0.3–5.4) ($n=7$) and 7.7 months (range 1.3–22.7) ($n=25$), respectively ($p=0.0017$). (B) Median OS of patients with absolute CD4+ ≤236 cells/mm³ versus >236 cells/mm³ was 2.7 months (range 0.3–6.7) ($n=9$) and 8.0 months (range 1.3–22.7) ($n=23$), respectively ($p=0.0029$). (C) Median OS of patients with absolute CD8+ ≤144 cells/mm³ versus >144 cells/mm³ was 2.7 months (range 1.2–5.4) ($n=5$) and 7.6 months (range 0.3–22.7) ($n=27$), respectively ($p=0.0313$). Data within the graphs were derived from Kaplan-Meier log-rank statistics and showed comparable results when compared to those from Wilcoxon's rank-sum test. OS overall survival. Wong et al. Dexamethasone exerts profound immunologic interference on treatment efficacy for recurrent glioblastoma. Br J Cancer. 113, 232–241, 2015

cacy after administration of just one dose. To make efficacy comparison between the two cohorts in EF-11 more biologically valid, the 27 suboptimally treated subjects were removed and the modified intent-to-treat cohorts consisted of 93 subjects treated with TTFields monotherapy and 117 subjects with chemotherapy [30]. Indeed, the modified TTFields monotherapy arm had a superior overall survival when compared to the chemotherapy arm, median 7.8 months versus 6.0 months, respectively, with a hazard ratio of 0.69 (95% CI 0.52–0.92) ($p=0.0093$, Fig. 6.5) [30].

Subgroup analyses were also performed in the EF-11 cohort to explore prognostic or predictive factors that may influence survival. First, TTFields treatment compliance significantly correlated with survival. The median overall survival was 5.8, 6.0, and 7.7 months for compliance rate of 40–59% ($n=10$), 60–79% ($n=22$), and 80–100% ($n=77$) ($p=0.039$) (Fig. 6.6) [30]. Second, in the intent-to-treat population, TTFields monotherapy was superior to chemotherapy among the subgroups with prior bevacizumab failure, low-grade glioma, tumor size ≥ 18 cm², and Karnofsky performance status ≥ 80 [30]. Lastly, subjects who received TTFields monotherapy ($n=120$) had longer survival compared to those who received bevacizumab-containing regimen ($n=33$), median overall survival 6.6 months versus 4.9 months, respec-

chemotherapy cohort that received dexamethasone ≤ 4.1 mg/day versus >4.1 mg/day. Subjects who took dexamethasone ≤ 4.1 mg/day ($n=63$) had a median tumor size of 4.2 (range 0.0–11.2) cm² as compared with those who used >4.1 mg/day ($n=54$) with a median tumor size of 9.6 (range 0.0–46.0) cm² ($p=0.1638$). BPC Best Physician's Choice, OS overall survival, TTFields Tumor Treating Fields, χ^2 chi-square. Wong et al. Dexamethasone exerts profound immunologic interference on treatment efficacy for recurrent glioblastoma. Br J Cancer. 113, 232–241, 2015.

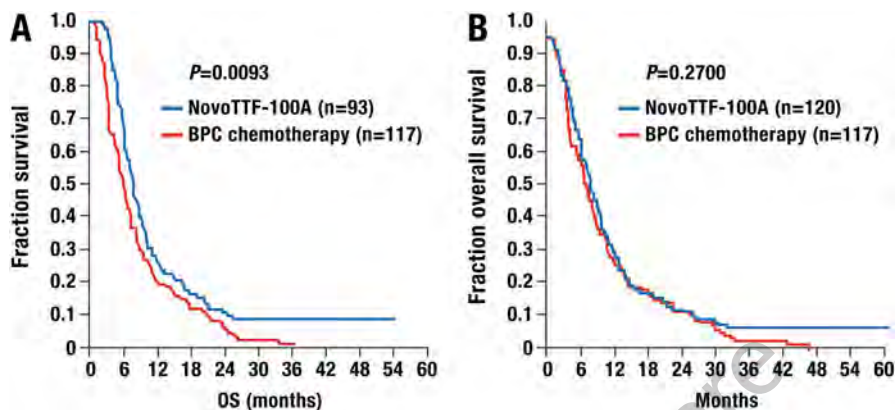


Fig. 6.5 Kaplan-Meier overall survival for (A) mITT and (B) ITT populations with recurrent glioblastoma treated with TTFields monotherapy or BPC chemotherapy in the EF-11 phase III trial. BPC best physician's choice, ITT intent to treat, mITT modified intent to treat. From Kanner et al. *Post Hoc* analyses of intention-to-treat population in phase III comparison of NovoTTF-100A™ system versus best physician's choice chemotherapy. *Semin Oncol.* 41:S25-S34, 2014. With permission from Elsevier

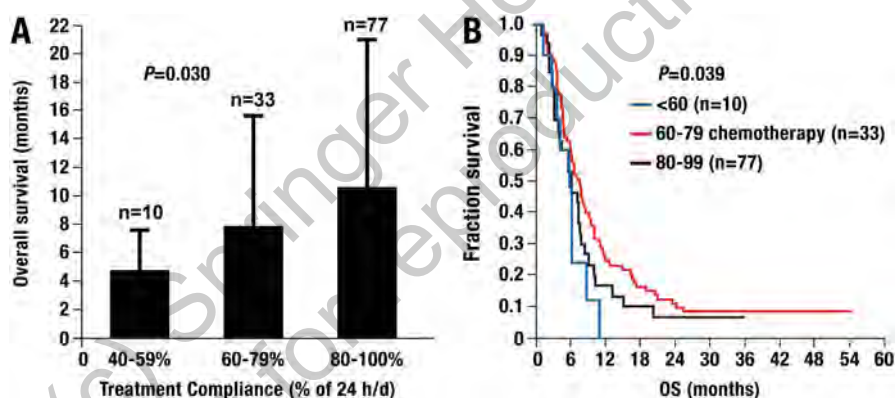


Fig. 6.6 *Post hoc* analysis of TTFields treatment compliance and survival in the EF-11 trial. (A) Spearman rank correlation between treatment compliance and mean OS showed a correlation coefficient of 0.175 (one-sided $p=0.030$). (B) Kaplan-Meier OS curves stratified according to compliance. There was a trend for longer median OS with better compliance, with median OS of 5.8 months for <60% compliance ($n=10$), 6.0 months for 60–79% compliance ($n=33$), and 7.7 months for 80–99% compliance ($n=77$) (log-rank test for trend, $\chi^2 p=0.039$). OS overall survival, χ^2 chi-square. From Kanner et al. *Post Hoc* analyses of intention-to-treat population in phase III comparison of NovoTTF-100A™ system versus best physician's choice chemotherapy. *Semin Oncol.* 41:S25-S34, 2014. With permission from Elsevier

tively, with a hazard ratio of 0.64 (95% CI 0.41–0.99) ($p=0.045$) [30] (Fig. 6.7). There was no difference in survival between TTFields monotherapy and non-bevacizumab chemotherapy ($n=84$): median overall survival 6.6 months versus 6.6 months, with a hazard ratio of 0.92 (95% CI 0.68–1.24) ($p=0.586$) [30].

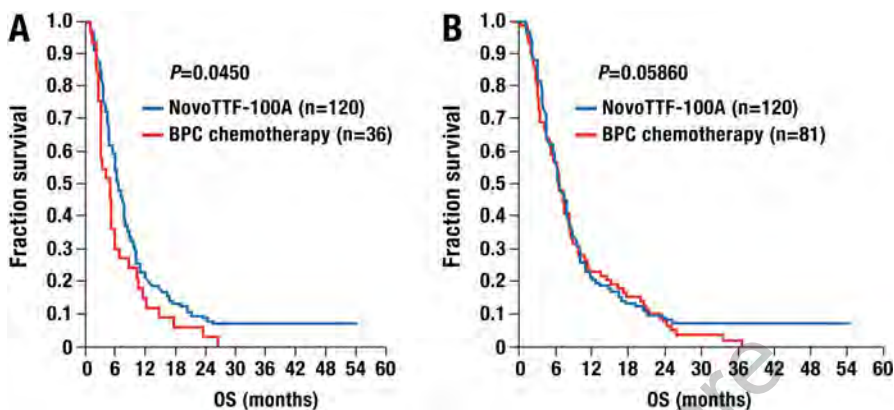


Fig. 6.7 *Post hoc* analysis of TTFields monotherapy versus bevacizumab and non-bevacizumab treatments. Overall comparison of Kaplan-Meier OS curves for ITT population with recurrent glioblastoma treated with TTFields monotherapy ($n=120$) versus (A) bevacizumab ($n=36$) or (B) non-bevacizumab ($n=81$) chemotherapy. ITT intent to treat, OS overall survival. From Kanner et al. Post Hoc analyses of intention-to-treat population in phase III comparison of NovoTTF-100A™ system versus best physician's choice chemotherapy. *Semin Oncol.* 41:S25-S34, 2014. With permission from Elsevier

Conclusions

The Optune® device delivered TTFields as treatment for recurrent glioblastoma in the pilot study and the EF-11 phase III trial. In the smaller pilot study, favorable survival characteristics were observed in 10 participants treated with TTFields. However, the subsequent phase III EF-11 trial showed only comparable efficacy when TTFields monotherapy was compared to Best Physician's Choice chemotherapy. The U.S. Food and Drug Administration nevertheless approved the use of the device in this population on April 8, 2011, based on the comparable efficacy, superior safety profile, and a better quality of life. Later, multiple *post hoc* analyses were performed and revealed a number of important findings that explains the discrepancy between the robust data from the pilot study and the results in the phase III trial. First, 27 (23 %) subjects did not receive a complete cycle of TTFields monotherapy and, when these subjects were removed from comparison with those treated with chemotherapy in the modified intent-to-treat analysis, TTFields were found to be superior to chemotherapy. Indeed, TTFields treatment compliance of 75 % or greater was later found to be significantly correlated with overall survival in the participants. Second, a higher dexamethasone dosage (>4.1 mg/day) used by some of the subjects had a negative effect on their survival outcome regardless of treatment with either TTFields or chemotherapy. Therefore, adhering to the recommended treatment compliance and minimizing the amount of daily dexamethasone intake will likely improve the outcome of patients treated with TTFields.

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Chapter 7

Tumor Treating Fields in Clinical Practice with Emphasis on PRiDe Registry

Jacob Ruzevick, Eric T. Wong, and Maciej M. Mrugala

Glioblastoma (GBM) is the most common primary malignant brain tumor in adults and is universally associated with a poor prognosis. Despite aggressive treatments consisting of maximal neurosurgical resection, chemotherapy, and radiation, patient outcomes remain poor with a median time to recurrence of approximately 7 months and a median overall survival of about 15 months [1, 2]. Following recurrence, the median progression-free survival and overall survival are approximately 9 weeks and 25 weeks, respectively [3]. The drug commonly used to treat patients with recurrent GBM is bevacizumab, which gained accelerated approval from the U.S. Food and Drug Administration in 2009 after two single-arm studies demonstrated a high radiologic response rate that was associated with improved clinical outcome [4–6]. While new drugs, such as small molecule tyrosine kinase inhibitors, monoclonal antibodies, and immune therapies, are rapidly changing the landscape of treatment options for GBM, this tumor inevitably develops resistance to systemic therapies. Therefore, multimodality treatment approach is critical for continued improvement of patient outcomes.

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Fig. 7.1 The Optune® device is comprised of transducer arrays that are placed on the scalp and connected to the field generator. This portable system is used in 4-week cycles with optimal results seen when compliance exceeds 75 % daily use (18 hours a day or more). Courtesy of Novocure



The Optune® device (Novocure Ltd., Haifa, Israel) was approved by the U.S. Food and Drug Administration in 2011 for use in patients with recurrent GBM [7]. The system is a portable, noninvasive device that delivers medium frequency (200 kHz) alternating electric fields, also known as Tumor Treating Fields (TTFields), directly to the tumor bed and peri-tumoral tissues. The unit can be carried in a compact backpack or used as a stationary unit with transducer arrays placed directly on the patient's scalp (Fig. 7.1). Unlike chemotherapeutics, which can exert anti-neoplastic activity long after dosing, TTFields therapy has no half-life, requiring that the device be worn continually in order to produce a beneficial anti-mitotic effect. A single "cycle" of TTFields therapy is 4 weeks of near continuous usage as this was shown to be the time course necessary for the electric fields to exert therapeutic effects on GBM [8]. The approval in the recurrent GBM population was based on the EF-11 phase III trial results in which 237 subjects were randomized in a 1:1 ratio to receive TTFields monotherapy versus best physician's choice chemotherapy [9]. The trial demonstrated that patient survival from TTFields was comparable to chemotherapy, while adverse event and quality of life analyses favored TTFields.

Clinical trials data may not always be representative of patient treatment outcome in a routine clinical practice environment. There are a number of reasons for that. First, upon trial entry, subjects must possess prespecified clinical characteristics that real-world patient may not have. As a result, trial subjects typically have better neurologic function, higher performance status, and fewer medical comorbidities, all of which may enable participants in the trial to benefit more from the new treatment. Second, the U.S. Food and Drug Administration must strike a fine balance between providing the public rapid access to new treatments for deadly diseases and requiring comprehensive data on their benefits and risks. This action sometimes results in the reversal of prior accelerated approval decisions for oncologic therapies. For example, approvals for bevacizumab in breast cancer and

gefitinib for non-small cell lung cancer was reversed after additional efficacy data showed no benefit [10–14]. Furthermore, after the accelerated approval of bevacizumab for recurrent GBM, two large-scale randomized phase III trials testing this drug in newly diagnosed patients did not show survival benefit [15, 16]. Therefore, bevacizumab’s indication for GBM is also at risk of withdrawal. Lastly, oncologists and other medical practitioners may have inherent beliefs, either conscious or subconscious, that may bias them toward not adapting the new treatment despite available evidence [17]. Therefore, post-approval registry may provide valuable information on the pattern of usage and the efficacy of new therapy in the real-world setting.

Real World Clinical Experience with Tumor Treating Fields

The efficacy of TTFields in recurrent GBM has been shown in prospective studies with the most important one being a phase III randomized clinical trial comparing TTFields monotherapy to physician’s best choice of chemotherapy (the EF-11 trial). A summary of clinical studies of TTFields in GBM is shown in Table 7.1. The results of these studies are discussed in Chapter 6.

Table 7.1 Baseline patient characteristics in PRiDe and EF-11 trial.

Patient characteristics		PRiDe TTFields therapy (n=457)	EF-11 TTFields therapy (n=120)	EF-11 chemotherapy (n=117)
Age (years)	Median (range)	55 (18–86)	54 (24–80)	54 (29–74)
Gender	Male	67.6%	77%	62%
	Female	32.4%	23%	38%
KPS	Median (range)	80 (10–100)	80 (50–100)	80 (50–100)
	10–60	19.0%	NA	NA
	70–80	46.6%	NA	NA
	90–100	30.9%	NA	NA
	Unknown	3.5%	NA	NA
Recurrence	Median (range)	2 (1–5)	2 (1–5)	2 (1–4)
	First	33.3%	9%	15%
	Second	26.9%	48%	46%
	Third to fifth	27.4%	43%	39%
	Unknown	12.5%	0%	0%
Prior treatments	Bevacizumab	55.1%	19%	18%
	RT+temozolomide	77.9%	86%	82%
	Debulking surgery	63.9%	79%	85%
	Carmustine wafers	3.7%	NA	NA

KPS Karnofsky performance status, NA not available, RT radiotherapy

Patient Registry Dataset (PRiDe)

As the Optune® device became available after U.S. Food and Drug Administration approval in clinical neuro-oncology practices, the PRiDe registry was set up in late 2011 to collect data on patients who were treated with TTFields for recurrent GBM [18]. From October 2011 thru November 2013, data on 457 patients were captured from 91 neuro-oncology centers or oncology practices certified to administer the device in the United States. All patients provided informed consent to allow their protected health information to be used for this registry. They also had a histologically confirmed diagnosis of GBM and recurrence was defined radiologically according to the Macdonald criteria [19]. Unlike patients in the pivotal phase III study, there were no exclusions based on previous radiation or chemotherapy regimens. Baseline clinical characteristics of patients were tabulated by chart review. Centralized collection of compliance data, which contain the cumulative amount of time therapy was delivered to the patient, were obtained by Novocure from an internal log file downloaded from each device. Compliance data was only available for two-thirds of participants because Novocure only started collecting this information centrally in January of 2013. Patient compliance was calculated as the average percentage of each day or a 24-hour period that the device was delivering TTFields. Prognostic factors such as age, Karnofsky performance status, debulking surgeries, the number of prior GBM recurrences, and prior bevacizumab use were captured for analysis. Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE). Patient survival information was captured using the United States Social Security Death Date Registry and obituaries.

There are a number of differences between participants in PRiDe and the TTFields monotherapy cohort in the EF-11 trial [9, 18]. First, patients who received the device in PRiDe were not restricted to TTFields treatment only. However, information on combined use of the device with other chemotherapies and/or bevacizumab, which was at the discretion of the treating physician, was not captured. In addition, some of the patients included in PRiDe could have been exhibiting pseudoprogression following combined chemotherapy and radiation, a known radiographic phenomenon that typically occurs within the first 12 weeks after treatment [20]. Second, as mentioned above, compliance data were captured from only about two-thirds of the patients. Lastly, PRiDe did not capture data on quality of life measures. Although these differences may make comparisons between the two groups of patients challenging, PRiDe nonetheless offers a unique opportunity to examine treatment efficacy and toxicities of the Optune® device in a real-world practice environment.

Patient Characteristics and Survival Differences Between PRiDe and EF-11

Baseline patient characteristics from PRiDe and comparison to the two cohorts in EF-11 are shown in Table 7.2. Among the 457 participants in PRiDe, the average age was 55 years (range 18–86) and approximately a third of them were women.

Table 7.2 Summary of clinical trials in GBM involving TTFields.

Study	n	Pathology	Study treatment	Median overall survival		Progression-free survival	
				TTFields	Chemotherapy	TTFields	Chemotherapy
Kirson et al. 2007 [24]	10	Recurrent GBM	TTFields only	14.4 months	–	6.0 months	–
Stupp et al. 2012 [8]	237	Recurrent GBM	TTFields vs best physician's choice chemotherapy	6.6 months	6.0 months	2.2 months	2.1 months
Mrugala et al. 2014 [18]	457	Recurrent GBM	TTFields ± chemotherapy	9.6 months			

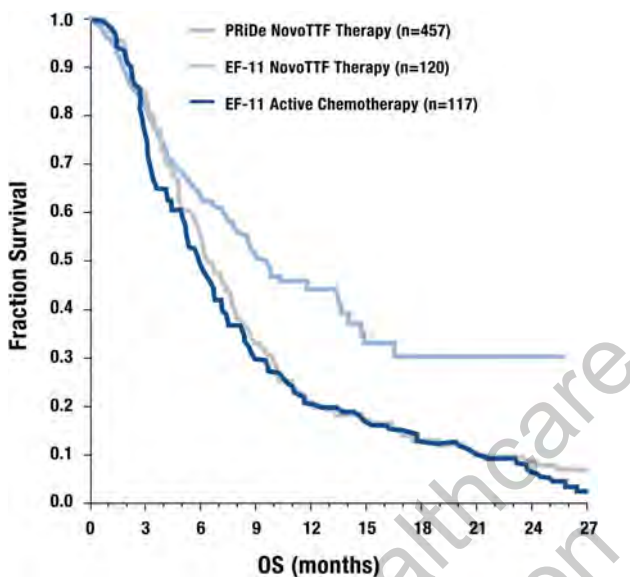


Fig. 7.2 Kaplan-Meier estimate of overall survival (OS) curves for patients with recurrent GBM treated with TTFields in PRiDe versus those received TTFields monotherapy or best physician's choice chemotherapy in the EF-11 trial. From Mrugala et al. Clinical practice experience with NovoTTF-100A™ system for glioblastoma: The Patient Registry Dataset (PRiDe). *Semin Oncol.* 41 Suppl 6: S4-S13, 2014. Elsevier

The median Karnofsky performance status was 80 (range 10–100). The median number of GBM recurrences prior to entry into PRiDe was 2 (range 1–5). Fifty-five percent of patients had previously been treated with bevacizumab, which is a greater number of patients than the 19% in the EF-11 TTFields monotherapy arm. Approximately 78% of them had received previous radiation and chemotherapy while 63% had debulking surgery.

A major finding in PRiDe is that the median overall survival in patients treated in clinical practice was improved as compared to TTFields monotherapy in the EF-11 phase III trial, 9.6 months versus 6.6 months respectively (Table 7.2 and Fig. 7.2), even though these two groups are not statistically comparable [18, 21, 22]. This favorable survival trend also extended out to the 2-year timeline with a respective survival rate of 30% versus 9% (Table 7.3) [18]. The improved survival among the patients in PRiDe may be due to a greater number (33%) starting treatment at the first recurrence, and fewer (27%) receiving it at third to fifth recurrences, as compared to only 9% and 43% respectively in EF-11. While the patients included in the PRiDe were more diverse and heterogeneous, they received a significantly longer duration of treatment as compared to those treated in EF-11, 4.1 months versus 2.3 months respectively [18]. Approximately 10% of those patients in the PRiDe continued on TTFields treatment for at least 2 years.

Table 7.3 One- and 2-year overall survival rates for patients with recurrent glioblastoma multiforme treated with TTFields therapy in PRiDe and EF-11 trial, and with best physician’s choice chemotherapy in the EF-11 trial

Endpoint	PRiDe TTFields therapy (n=457)	EF-11 TTFields therapy (n= 120)	EF-11 chemotherapy (n= 117)
1-Year survival	44 %	20 %	20 %
2-Year survival	30 %	9 %	7 %

Table 7.4 Summary of dermatologic adverse events in clinical studies involving TTFields.

Study	n	Pathology	Study treatment	Dermatologic AE
Kirson et al. 2007 [24]	10	Recurrent GBM	TTFields only	90 %
Stupp et al. 2012 [9]	237	Recurrent GBM	TTFields vs. best physician’s choice chemotherapy	Grade I/II: 16 % Grade III/IV: 3 %
Mrugala et al. 2014 [18]	457	Recurrent GBM	TTFields ± chemotherapy	24 %

No Unexpected Adverse Events in PRiDe

The tolerability and safety of TTFields treatment in PRiDe were analyzed and no unexpected adverse events were found when compared to prior trials. The most common device-related side effects were skin reactions, heat sensations, and electric sensations on the scalp associated with the transducer arrays, occurring at a rate of 24 %, 11 %, and 8 %, respectively (Tables 7.4 and 7.5) [18]. Nervous system-related events were the second most common adverse events, and included neurological disorders (10 %), seizures (9 %), and headaches (6 %). Many of the nervous system-associated events were likely associated with the recurrent GBM [18].

Prognostic Factors in PRiDe

A number of prognostic factors were identified in the PRiDe population and they are displayed in Figs. 7.3 and 7.4. Similar to the prospective EF-11 study, compliance ≥75 % was notably associated with improved median overall survival when compared to <75 %, 13.5 months versus 4.0 months, with a hazard ratio of 0.4 (95 % CI 0.3–0.6) ($p < 0.001$, Fig. 7.3) [18]. This finding is consistent with device’s mechanism of action in that TTFields disrupt tumor cells during mitosis and the fields have to be present continuously in order to exert its anti-tumor effect. Other favorable prognostic factors included early introduction of therapy and higher Karnofsky performance status (Fig. 7.4) [18]. Patients who failed bevacizumab did not respond as well, most likely because of the more extensive infiltration of the brain by recurrent glioblastoma. Debulking surgery that was performed prior to the application of the device did not influence patient survival (Fig. 7.4).

Table 7.5 Adverse events in patients with recurrent glioblastoma treated with TTFields in PRiDe.

Adverse event	Percentage of patients PRiDe (n=457)
Skin reaction	24.3
Heat sensation	11.3
Neurological disorder	10.4
Seizure	8.9
Electric sensation	7.7
Headache	5.7
Pain/discomfort	4.7
Fall	3.9
Psychiatric disorder	2.9
Gastrointestinal disorder	2.9
Fatigue	2.5
Vascular disorder	1.6
Weakness	1.4
Infections	1.4
Eye disorder	1.3

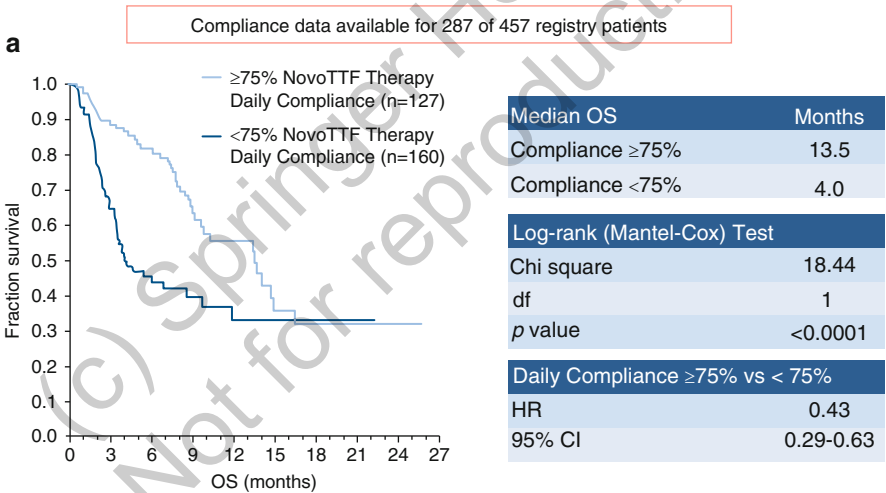


Fig. 7.3 Treatment compliance with TTFields. **(a)** Results from PRiDe with respect to overall survival by daily compliance, dichotomized according to $\geq 75\%$ versus $< 75\%$, with TTFields therapy for recurrent GBM. **(b)** Representative compliance report generated after a cycle of TTFields therapy. **(a)** From Mrugala et al. Clinical practice experience with NovoTTF-100A™ system for glioblastoma: The Patient Registry Dataset (PRiDe). Semin Oncol. 41 Suppl: S4-S13, 2014. Elsevier. **(b)** Courtesy of Novocure

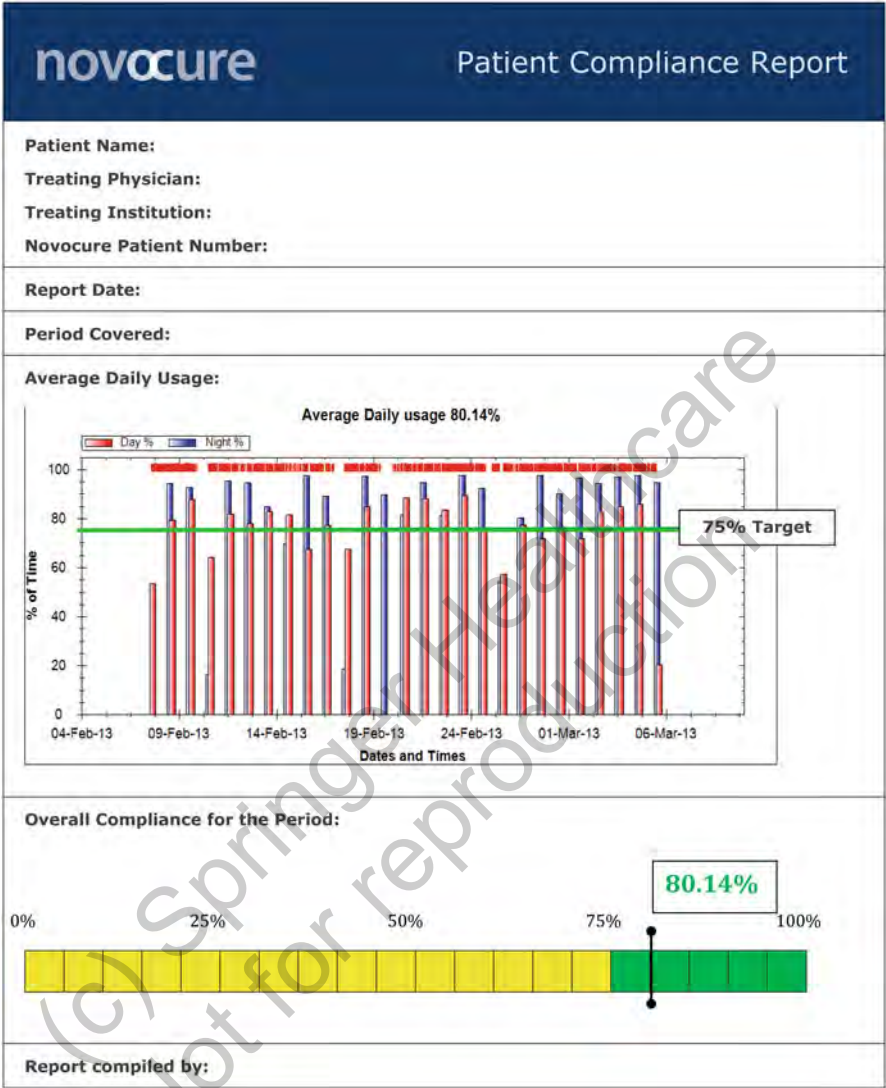


Fig. 7.3 (continued)

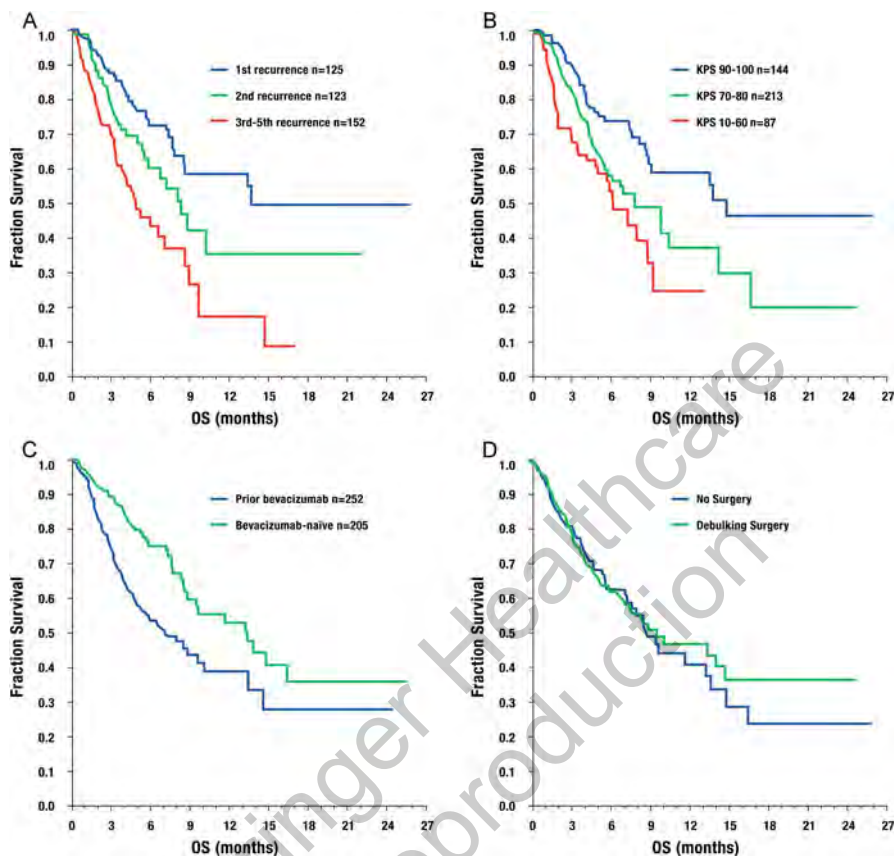


Fig. 7.4 Kaplan-Meier estimate of overall survival curves for patients with recurrent GBM treated with TTFields in PRiDe according to (A) recurrence number, (B) Karnofsky performance status, (C) prior bevacizumab use, and (D) prior debulking surgery. From Mrugala et al. Clinical practice experience with NovoTTF-100A™ system for glioblastoma: The Patient Registry Dataset (PRiDe). *Semin Oncol.* 41 Suppl 6: pp S4-S13, 2014. Elsevier

Special Clinical Considerations for Patients Treated with Tumor Treating Fields

One unique situation to consider in patients with GBM who might be candidates for TTFields therapy is the presence of intracranial hardware, such as shunts for cerebrospinal fluid diversion. While shunts with programmable valves were part of the exclusion criteria for EF-11, Mrugala et al. [23] reported that TTFields were used safely in a single patient with a nonprogrammable ventriculo-peritoneal shunt (Fig. 7.5). Since cerebrospinal fluid diversion is common in patients operated on for intracranial tumors, additional reports of the use of nonprogrammable shunts are needed to establish their safety in the setting of TTFields

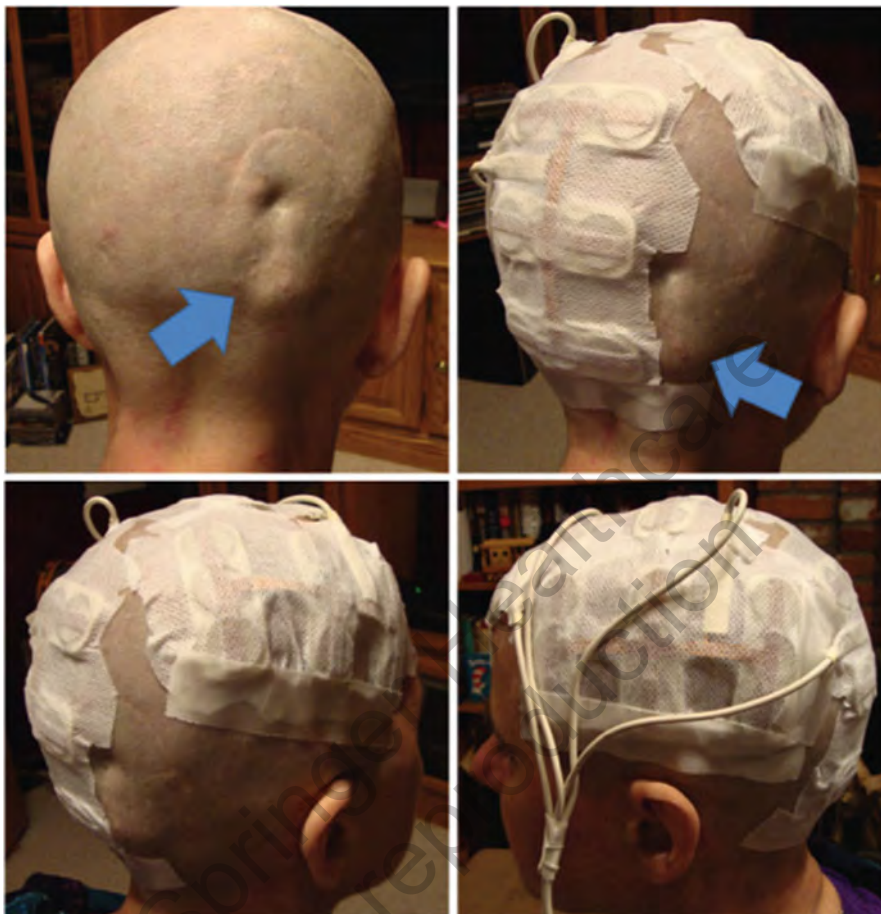


Fig. 7.5 The Optune® device was successfully utilized in a patient with ventriculo-peritoneal shunt and nonprogrammable valve. Arrows identify the valve in relationship to the treatment arrays. The patient used TTFields for over 12 months and experienced no complication.

application. Data pertaining to this issue are being actively collected and will be published in the near future.

Intensity of the electrical fields being applied to the tumor and the surrounding tissues heavily depends on the positioning of the treatment arrays on the scalp. In general, the closer the arrays are to each other, the higher the intensity of the fields and consequently greater efficacy of the anti-mitotic activity from the treatment. To identify the optimal positioning of the transducer arrays, the NovoTAL™ (transducer array layout) system was developed (Fig. 7.6). This system inputs magnetic resonance imaging of a gender-specific head morphology, tumor location, and size to optimize the intensity of TTFields directed at the tumor. The NovoTAL™ system, approved by the U.S. Food and Drug Administration for clinical use, allows treating physicians to generate treatment maps and adjust them accordingly during treatment when tumor-specific parameters change.



Fig. 7.6 NovoTAL™ system allows physicians to create treatment maps and customize TTFields therapy. The intensity of the electric fields can be modulated and optimized by changing the location of the transducer arrays. Courtesy of Novocure

Dermatologic Side Effects of Tumor Treating Fields Therapy

Hematologic and gastrointestinal toxicities frequently seen in association with chemotherapeutics are not encountered with TTFields therapy. Given the mode of administration through the direct placement of treatment arrays on the skin, dermatologic complications were the most commonly seen side effect in all reported clinical studies [9, 18]. Skin-related complications resulting from the use of the device include dermatitis, erosions, infections, and ulcers. Most of these complications are likely a result of mechanical trauma from repeated application of arrays, poor wound healing, and potentially combination treatment with chemotherapeutics. Dermatologic complications of TTFields treatment will be discussed in detail in Chapter 9.

Conclusions

GBM is one of the most difficult cancers to treat and surgical resection, radiation, and systemic chemotherapy do not offer a cure. TTFields represent a novel and unique treatment method. This anti-mitotic device is externally worn on the scalp and is not associated with the typical systemic side effects seen with chemotherapy. The pivotal randomized phase III clinical trial showed a median overall survival of 6.6 months in recurrent GBM subjects, similar to what can be achieved with

standard chemotherapies but with fewer side effects. PRiDe is a large registry of 457 patients with recurrent glioblastoma treated with TTFields therapy in routine clinical practice after approval by the U.S. Food and Drug Administration in 2011. Even though this registry cannot be directly compared to the randomized prospective trial, outcome data from this dataset provide an important adjunct in assessing the true efficacy of the device. Key findings from PRiDe include a significantly longer overall survival as compared to the TTFields monotherapy cohort in the EF-11 phase III trial and excellent tolerability. Favorable prognostic factors include good treatment compliance and higher Karnofsky performance status. Moreover, data from PRiDe indicate that earlier introduction (at first progression) of treatment may result in improved outcomes in recurrent GBM and that bevacizumab-naïve patients benefit from TTFields more than patients previously treated. Patient compliance with this continuous anti-cancer therapy is critical as increased usage (18 hours per day or more) is associated with improved survival. The reasons for the difference in outcomes between the EF-11 clinical trial and the PRiDe dataset are not fully understood. Several factors, discussed above, might have played a role and these include combination therapies and potential pseudoprogression issue in PRiDe, as well as selection bias towards worse performing subjects in the EF-11 trial. Nevertheless, patients in PRiDe collectively appear to perform better than those enrolled in EF-11 and this dataset offers an important view of TTFields treatment efficacy in the real-world setting.

The Optune® device can be safely and effectively used in the clinical practice setting after appropriate training and credentialing process is completed. The NovoTAL™ platform allows physicians to customize therapy to the individual patient and adjust treatment planning during the course of therapy. Ultimately, physician experience accumulated during clinical practice will improve the clinical application of this device.

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Chapter 8

Tumor Treating Fields Therapy for Newly Diagnosed Glioblastoma

Eric T. Wong and Zvi Ram

Glioblastoma is a heterogeneous disease. From a molecular perspective, multiple mutations are found in various signal transduction pathways, including those in the canonical phosphoinositol-3-kinase/mitogen-activated protein kinase pathways that regulate growth and survival, the p53 transcription factor that governs senescence and apoptosis, as well as the retinoblastoma/cyclin-dependent kinase regulatory pathway that controls the cell cycle [1]. At least four molecular subtypes of glioblastoma can be characterized at initial diagnosis and defined according to gene expression profiling as proneural, neural, classical, and mesenchymal subtypes [1, 2]. These glioblastoma subtypes have different responsiveness to treatments; patients with classical and mesenchymal characteristics lived longer when treated with intensive radiotherapy and temozolomide while those with the proneural subtype did not [2]. Further complicating the molecular landscape is the multitude of amplified and mutated genes within each tumor cell. For example, amplifications and mutations of multiple receptor tyrosine kinases and other downstream signaling kinases that regulate key cellular processes are found in varying degrees in individual tumor cells, which eventually give rise to subpopulations with more heterogeneous amplifications and mutations [3–5]. Collectively, these inter-tumoral and intra-tumoral heterogeneities, as well as the tendency to acquire additional mutations as a result of cancer evolution or treatment, invariably make glioblastoma very difficult to control.

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The clinical behavior of glioblastoma is multifaceted. Tumor growth and proliferation, angiogenesis and invasion are the clinical hallmarks of this disease, but the extent to which each hallmark appears in individual patients is variable [6]. Furthermore, although the glioblastoma is often detected as a solitary mass at initial diagnosis, some are more invasive than others and appear in a gliomatosis fashion [7]. It can also present in a multifocal pattern, either synchronously with the primary tumor or metachronously as additional foci emerge after initial diagnosis and treatment [8]. Whether or not each individual focus is clonally related is unclear. Under rare circumstances, glioblastoma can even metastasize outside the central nervous system, and this is made possible by the presence of circulating tumor cells [9, 10].

The extensive heterogeneity in the glioblastoma's molecular makeup and clinical behavior presents a daunting challenge in constructing effective treatment regimens for this disease. The tumor also co-opts normal physiological processes, such as angiogenesis and immune tolerance, to subserve its own survival and proliferation within the patient. An obvious strategy is to block deranged intra-tumoral processes, such as amplified or mutated receptor tyrosine kinases and other downstream kinases that are targets for small molecule inhibitors or monoclonal antibodies, but none have yet been shown to benefit glioblastoma patients [11, 12]. Strategies that reverse or normalize co-opted physiological processes may have a chance because these processes are probably less disordered and more amenable to intervention. For example, bevacizumab, which normalizes tumor blood vessels, has been shown to prolong progression-free survival but not overall survival in newly diagnosed patients [13–15]. Furthermore, gross total neurosurgical resection of the glioblastoma provides a means of significant cytoreduction. This cytoreduction not only diminishes the intracranial mass effect that may debilitate patients but also reduces the number of heterogeneous cell types that are resistant to subsequent radiation and chemotherapy. In addition, because loss of *Phosphatase and Tensin Homolog (PTEN)* activates glioblastoma-induced immune suppression, reduction of *PTEN* null or mutated tumors can potentially reduce the tumor's ability to evade the immune system [16, 17]. Lastly, dexamethasone has beneficial anti-edema effects in the brain but it also interferes with immune effector functions against the glioblastoma, as shown in past *post hoc* analyses of the EF-11 trial comparing Tumor Treating Fields (TTFields) with chemotherapy and retrospective analysis of patient outcome from radiation treatment [18–20]. Regardless of the etiology, a drop in the CD4⁺ lymphocyte counts to <200 cell/mm³ is correlated with a poorer survival compared to ≥200 cell/mm³, suggesting that CD4⁺ count may serve as a marker of immune competence in the glioblastoma population [21]. A dexamethasone dose <4 mg/day probably provides some anti-edema benefit in patients while not interfering with their immune effector function against the glioblastoma [18, 22]. Alternatives to dexamethasone include bevacizumab, celecoxib, and angiotensin receptor blockers [23–26] that are not thought to interfere with the immune system. Taken together, strategies that block co-opted physiological processes by the glioblastoma, as well as those that accentuate the patient's own anti-tumor response, are more likely to be met with success (Fig. 8.1).

TTFields are a new cancer treatment that can interfere with the co-opted cell division machinery and potentiate anti-tumor immune response. Specifically, the

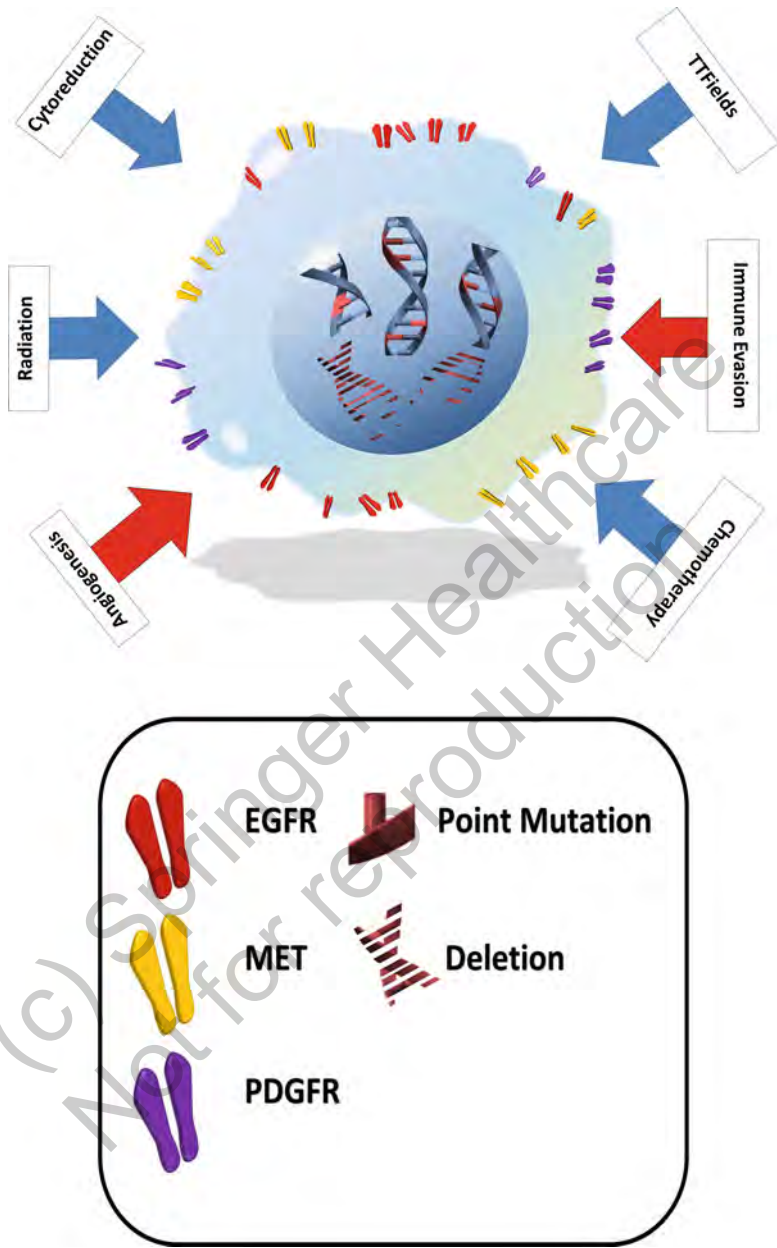


Fig. 8.1 Glioblastoma tumor cells have amplifications and mutations of multiple receptor tyrosine kinases and other downstream signaling kinases. Angiogenesis and immune tolerance are normal physiological processes that are co-opted by the tumor cells for their own growth and proliferation. Therefore, treatment strategies that reverse the co-opted physiological processes, like cytoreduction, radiation, chemotherapy, and TTFields, can potentially provide control of the glioblastoma.

alternating electric fields at frequencies ranging from 100 to 300 kHz disrupt tumor cell cytokinesis during mitosis that results in asymmetric chromosome segregation, aberrant mitotic exit, and immunogenic cell death [27–29]. TTFields monotherapy was compared to chemotherapy for recurrent glioblastoma and the phase III trial showed equivalent efficacy between these two disparate treatment modalities [30]. But patients treated with TTFields experienced fewer adverse events and a better quality of life [30]. Furthermore, the efficacy of TTFields has also been put to test in the newly diagnosed glioblastoma patients. In this chapter, the up-to-date results of the pivotal phase III trial for this population are described.

Pilot Study of Tumor Treating Fields in Newly Diagnosed Glioblastoma

A pilot study to test the safety of TTFields therapy was conducted from 2005 to 2007 in ten patients with newly diagnosed glioblastoma [31]. The median age of this cohort was 50 (range 32–70) years. All subjects possessed a Karnofsky performance status of 70 or greater and the median Karnofsky was 90. The median overall survival of the cohort was about 56 months and there were two long-term survivors. The first long-term survivor received TTFields and maintenance temozolomide for 12 months, after initial standard radiotherapy and concomitant daily temozolomide. This patient did not develop tumor recurrence and lived for at least another 59 months thereafter [31]. The second long-term survivor was also treated with TTFields and maintenance temozolomide for 12 months, and continued to have no tumor recurrence and lived for an additional 53 months [31]. It is notable that both patients were young, 32 and 33 years respectively, and younger patients are likely to be more responsive to treatment and live longer. In addition, the observed anti-tumor efficacy supports preclinical data demonstrating an *in vitro* synergistic effect of TTFields with various chemotherapeutic agents in multiple cancer types [32].

EF-14 was the Second Randomized Trial Using Tumor Treating Fields

This phase III trial enrolled 695 of the planned 700 subjects in a 2:1 ratio between 2009 and 2014, comparing TTFields plus maintenance temozolomide ($n=466$) with temozolomide alone ($n=229$) [33]. The primary outcome measure was progression-free survival and secondary endpoints were overall survival, progression-free survival at 6 months, percent 1- and 2-year survival, radiological response based on Macdonald criteria, quality of life assessment (EORTC QLQ-C30) and adverse events severity and frequency [33, 34]. The results of the pre-specified interim analysis have been published, which occurred after 210 subjects were randomized to TTFields plus temozolomide and 105 randomized to temozolomide alone, and was

conducted after a median follow-up of 38 (range 18–60) months [35]. Baseline clinical characteristics were balanced and the respective (i) median age was 55 and 57 years, (ii) male:female ratio was 2.0 and 1.8, (iii) corticosteroid use was 24 % and 25 %, (iv) percent completed standard 60 Gy radiotherapy was 91 % and 95 %, and (v) the median number of maintenance temozolomide cycles received was 6 and 4 (Table 8.1) [33, 35]. Both groups had aggressive tumor cytoreduction, and nearly two-thirds of patients underwent gross total resection while another quarter had partial resection [35]. The primary efficacy end-point analysis demonstrated improvement in progression-free survival in the intent-to-treat population of the

Table 8.1 Baseline patient characteristics and treatment details.

	All patients (N=315)	TTFields plus Temozolomide (n=210)	Temozolomide alone (n=105)
Age (years)			
Mean (SD)	55.8 (11.1)	55.3 (11.3)	56.8 (10.5)
Median (range)	57 (20–83)	57 (20–83)	58 (21–80)
Karnofsky Performance Status score, median (range), % ^a	90 (60–100)	90 (60–100)	90 (70–100)
Gender, no. (%)			
Male	207 (66)	140 (67)	67 (64)
Female	108 (34)	70 (33)	38 (36)
Use at baseline, no. (%)			
Antiepileptic medication	126 (40)	88 (42)	38 (36)
Corticosteroid therapy	77 (24)	51 (24)	26 (25)
Mini-Mental State Examination score, no. (%) ^b			
≤26	45 (15)	31 (15)	14 (13)
27–30	247 (78)	174 (83)	73 (70)
Unknown	23 (7)	5 (2)	18 (17)
Extent of resection, no. (%)			
Biopsy	34 (11)	23 (11)	11 (10)
Partial resection	79 (25)	52 (25)	27 (26)
Gross total resection	202 (64)	135 (64)	67 (64)
Tissue available and tested, no. (%)			
MGMT methylation	75 (33)	49 (32)	26 (35)
No methylation	116 (51)	79 (52)	38 (51)
Invalid test result	36 (16)	24 (16)	11 (15)
Region, no. (%)			
United States	191 (61)	127 (60)	64 (51)
Rest of world	124 (39)	83 (40)	41 (39)
Completed radiation therapy, no. (%)			
<57 Gy	18 (6)	13 (6)	5 (5)
60 Gy (standard ± 5 %)	291 (92)	191 (91)	100 (95)
>63 Gy	6 (2)	6 (3)	0 (0)

(continued)

Table 8.1 (continued)

	All patients (<i>N</i> =315)	TTFields plus Temozolomide (<i>n</i> =210)	Temozolomide alone (<i>n</i> =105)
Concomitant temozolomide use, no. (%)			
Yes	308 (98)	207 (99)	101 (96)
Unknown	7 (2)	3 (1)	4 (4)
Time from event to randomization, median (range), days			
Last day of radiotherapy	37 (13–68)	36 (13–53)	38 (13–68)
Initial diagnosis	114 (43–171)	115 (59–171)	113 (43–170)
No. of maintenance temozolomide cycles until first tumor progression, median (range)	6 (1–26)	6 (1–26)	4 (1–24)
Duration of treatment with TTFields, median (range), months	9 (1–58)	9 (1–58)	
Adherence to TTFields therapy ≥75 % during first 3 months of treatment		157 (75)	

MGMT 0⁶-methylguanine-DNA methyltransferase, *TTFields* Tumor Treating Fields

^aA higher score indicates better functional status

^bA higher score indicates better cognitive capability

defined interim-analysis dataset and after a median follow-up of 38 months. The median progression-free survival from randomization was 7.1 (95 % CI 5.9–8.2) months in the TTFields plus temozolomide cohort and 4.0 (95 % CI 3.3–5.2) months in the temozolomide alone cohort (hazard ratio=0.62 [95 % CI 0.43–0.89], *p*=0.001) (Fig. 8.2A). In secondary endpoint analyses, the overall survival of the intent-to-treat population showed a median overall survival of 19.6 (95 % CI 16.6–24.4) months in the TTFields plus temozolomide group versus 16.6 (95 % CI 13.6–19.2) months in the temozolomide alone group (hazard ratio=0.74, [95 % CI 0.56–0.98], *p*=0.03) (Fig. 8.2B). The percent of patients alive at 2 years was 43 % and 29 %, respectively (*p*=0.006). When compared to EF-11, the robust efficacy data from EF-14 support the notion that the clinical efficacy of an anti-mitotic treatment, like TTFields, will be more apparent when applied to patients who have undergone aggressive cytoreduction of the tumor, limited use of dexamethasone, and received treatment at an earlier time point of the disease. As patients were allowed to continue the use of TTFields even when tumor recurrence was observed, the data also suggest that extended treatment may still exert an anti-tumor effect even after tumor progression.

Safety and tolerability analysis showed no unexpected grade 3 or 4 adverse events, with nervous system and hematologic events being most common (Table 8.2) [35]. Twenty-two percent of the subjects who received TTFields plus temozolomide (*n*=203) experienced nervous system events, with 7 % seizure and 2 % headache, compared to 25 % who received temozolomide alone (*n*=101), with 8 % seizure and 2 % headache. The respective hematologic disorders were 12 % and 9 %, with 9 % and 3 % thrombocytopenia, 3 % and 1 % neutropenia, 5 % and 5 % leukopenia or lympho-

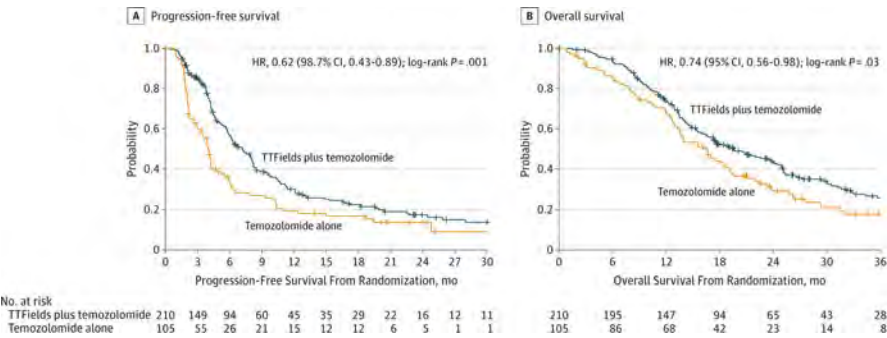


Fig. 8.2 Survival curves for patients included in the interim analysis in the intent-to-treat population. Survival analyses on time from date of randomization until tumor progression, death, or last follow-up (censored patients) according to the Kaplan-Meier method. **(A)** Progression-free survival and **(B)** overall survival. The small vertical ticks on the curves indicate censored patients. HR hazard ratio, TTFIELDS Tumor Treating Fields

Table 8.2 Grade 3 to 4 treatment-emergent adverse events.

	No. (%) of Patients With Adverse Events ^a	
	TTFIELDS Plus Temozolomide (n = 203) ^b	Temozolomide Alone (n = 101) ^c
Hematological disorders ^d	25 (12)	9 (9)
Anemia	1 (<1)	2 (2)
Leukopenia or lymphopenia	11 (5)	5 (5)
Neutropenia	6 (3)	1 (1)
Thrombocytopenia	19 (9)	3 (3)
Cardiac disorders	2 (1)	3 (3)
Eye disorders	2 (1)	1 (1)
Gastrointestinal disorders ^d	11 (5)	2 (2)
Abdominal pan	2 (1)	0
Constipation	2 (1)	0
Diarrhea	1 (<1)	2 (2)
Vomiting	3 (1)	1 (1)
General disorders	17 (8)	5 (5)
Fatigue	8 (4)	4 (4)
Infections	10 (5)	5 (5)
Injury and procedural complications ^d	14 (7)	5 (5)
Fall	6 (3)	2 (2)
Medical device site reaction	4 (2)	0
Metabolism and nutrition disorders	7 (3)	3 (3)
Musculoskeletal disorders	8 (4)	3 (3)
Nervous system disorders ^d	45 (22)	25 (25)
Seizure	15 (7)	8 (8)
Headache	4 (2)	2 (2)

(continued)

Table 8.2 (continued)

	No. (%) of Patients With Adverse Events ^a	
	TTFields Plus Temozolomide (n = 203) ^b	Temozolomide Alone (n = 101) ^c
Psychiatric disorders ^d	9 (4)	3 (3)
Anxiety	2 (1)	0
Bradyphrenia	0	1 (1)
Confusional state	2 (1)	1 (1)
Mental status changes	4 (2)	1 (1)
Psychotic disorder	2 (1)	0
Respiratory disorders	4 (2)	1 (1)
Skin disorders	0	1 (1)
Vascular disorders ^d	8 (4)	8 (8)
Deep vein thrombosis	1 (<1)	3 (3)
Pulmonary embolism	4 (2)	6 (6)

TTFields, Tumor Treating Fields

^aSafety is reported on patients who have received any treatment. Randomized patients who never received any maintenance therapy were excluded from this safety analysis

^bEight patients died while receiving adjuvant therapy due to causes unrelated to therapy (1 patient for each of the following reasons: cardiac events, pulmonary emboli, respiratory, and infection; and 4 patients with central nervous system disorders likely due to tumor progression)

^cFour patients died while receiving adjuvant therapy due to causes unrelated to therapy (1 patient for each of the following reasons: cardiac events, pulmonary emboli, respiratory, and unknown)

^dPatients may have had more than 1 adverse event so subcategories do not total and not all events are subcategorized

penia, and <1 % and 2 % anemia. Site reaction occurred in 2 % of device-treated subjects while 0 % in temozolomide alone subjects, and falls occurred in 3 % and 2 % of the subjects respectively. Therefore, TTFields therapy combined with temozolomide was well-tolerated and exhibited no new side effect from the combination.

Conclusions

Glioblastoma has significant inter-tumoral and intra-tumoral heterogeneity in molecular characteristics and clinical behavior. Therefore, the prerequisites to demonstrating the clinical efficacy of TTFields are probably related to gross total neurosurgical resection for the purpose of tumor cytoreduction, limited use of immunosuppressive dexamethasone, and intervention at an earlier time point of the disease. Indeed, when TTFields therapy was combined with maintenance temozolomide in the EF-14 phase III trial, the combination was demonstrated to have superiority in both progression-free survival and overall survival when compared to temozolomide alone. Furthermore, the combination was not associated with new or unexpected adverse events. Therefore, the collective data indicate that TTFields treatment, as delivered by the Optune® device, is an important treatment modality for glioblastoma patients.

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Chapter 9

Supportive Care in Patients Using Tumor Treating Fields Therapy

Mario E. Lacouture, John DeNigris, and Andrew A. Kanner

Optune® is a cancer treatment device that uses alternating electric fields or Tumor Treating Fields (TTFields) to provide local therapy for a patient's tumor. It has received approval for two indications from the U.S. Food and Drug Administration, the first in 2011 for recurrent glioblastoma and the second in 2015 for newly diagnosed glioblastoma. The initial approval in patients with recurrent glioblastoma was based on the device's (i) comparable treatment efficacy when compared to systemic chemotherapy, (ii) absence of serious adverse events, and (iii) improved quality of life (QoL) [1, 2]. Furthermore, no new or unexpected adverse events were noted in the post-approval patient registry [3]. The second approval resulted from favorable progression-free survival and overall survival in the device-treatment arm in combination with maintenance temozolomide after a pre-specified interim analysis [4]. There was also no unexpected adverse event and the QoL outcome appeared to be similar in both arms. However, dermatologic adverse events (dAEs) remain an important issue among patients receiving TTFields therapy. In this chapter, the prevention, diagnosis, and management of dAEs are discussed in the first section while the QoL analyses from both pivotal phase III clinical trials are reviewed in the second section.

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Dermatologic Adverse Events Associated with Tumor Treating Fields Therapy

TTFields are delivered by ceramic discs located on two pairs of transducer arrays. These discs have a layer of hydrogel to ensure conductive contact with the scalp and they are adherent to the patient's shaved head by hypoallergenic medical tape. While systemic adverse events have not been reported, the continuous application of the transducer arrays results in a new category of dAEs, with contact dermatitis and skin infections being the most prominent ones [2]. Knowledge of the mechanisms by which these dAEs develop, as well as strategies for prevention and treatment are critical to maintain QoL and consistency of device utilization.

Pathophysiology of Dermatologic Adverse Events

The epidermis is composed of keratinocytes, melanocytes, Langerhans cells, and Merkel cells. The doubling time of human keratinocytes is every 24 hours, with transit time from the basal layer to the stratum corneum taking at least 14 days. Further transit from the stratum corneum to desquamation requires an additional 14 days [5] and therefore a complete turnover of the epidermis takes a total of 28 days. Cells from the innate arm of the immune system, including macrophages, antigen-presenting cells, and natural killer cells reside in the epidermis. When there is an insult to the skin, lymphocytes from the adaptive immune system may temporarily take residence in the epidermis. These immune cells are responsible for the observed contact dermatitis that may develop upon exposure to some of the components of the Optune® device.

Transducer arrays are directly applied to the scalp for at least 18 hours a day and left in place for 3 to 4 days at a time. During an array exchange, the previous ones are removed and new ones are placed on the scalp in a slightly relocated fashion to reduce prolonged direct contact. Distinctive mechanical, thermal, chemical, and moisture-related stresses occur if the arrays are applied repeatedly to the same area of the skin. Given the potential for causing dAEs, meticulous monitoring of the skin condition and timely exchange of the arrays are highly recommended.

Hair directly affects the quality of array-to-scalp contact. There are approximately 100,000 hair follicles on the scalp, and around 100 shafts of hair shed each day [6]. An outward pressure to the adhered transducers arrays is generated by a growth rate of 0.2 to 0.5 mm per day. To minimize the effect of this pressure, the scalp should be shaved every time when the arrays are exchanged.

Surgery will invariably result in the formation of a scar on the incised skin. Scars arise due to fibrous tissue proliferation during the replacement of previously normal skin where integrity is compromised. Although a scar continues to remodel for up to 1 year after surgical incision, the skin on the scar does not fully regain its original mechanical strength. It is estimated that scars have only 70 % of the tensile strength

of normal skin [7]. Moreover, altered circulation through scar tissue increases patient susceptibility to dAEs when ceramic discs are placed immediately over them [7].

Abnormal stimuli to the skin are the catalysts that produce pathological changes. TTFields therapy potentially exposes skin to stimuli such as repetitive mechanical trauma, resulting in inflammation, infection, and wound healing complications at the site of previous surgical scars. The shaved scalp that was previously covered by hair may be exposed to ambient ultraviolet radiation and this may result in inflammatory changes [7]. Multiple risk factors have been found to increase the risk of developing dAEs. The first would include placing the ceramic discs from the arrays directly over scars or craniotomy hardware. Another risk factor occurs in patients who have previously developed a contact dermatitis reaction to any materials that are in the arrays. Those with hyperhidrosis (excessive sweating) have been found to have a higher complication rate due to the hydrophilic nature of hydrogel, which may liquefy at high ambient temperature and upon exposure to sweat. Additionally, there is an increased risk for individuals with a history of skin exposure to radiation, either ultraviolet and/or ionizing radiation, and those who are also being treated with systemic anti-cancer agents, high doses of corticosteroid, or both [7].

Specific Dermatologic Pathologies

Five types of potential pathologies leading to dAEs have been noted with the use of TTFields therapy (Table 9.1), including (i) allergic contact dermatitis (ACD), (ii) irritant contact dermatitis (ICD), (iii) erosions, (iv) ulcers, and (v) skin infections or pustules [7]. These processes may occur independently or coexist at sites where the scalp makes contact with the arrays. Chemical irritation from the hydrogel, moisture and/or alcohol may directly lead to ICD, while allergy to the adhesive tape and/or hydrogel may cause a delayed form of ACD. Erosions from mechanical trauma may occur from shaving, array application, or array removal. Ischemic injury produced by pressure from the arrays may lead to ulcer formation. Ultimately, infection with or without pustules may occur when the skin is affected by pathogenic bacteria [7].

ACD and ICD are the two types of inflammation that patients may develop when using TTFields therapy [7]. ACD is characterized by an inflammatory reaction to specific exogenous allergens that come into contact with the skin. In this case, an individual must become sensitized to the allergen [8]. Resolution of ACD not only requires removing the allergen, but may also necessitate the use of topical corticosteroids to quell the inflammatory reaction. In contrast, ICD is a nonspecific type of inflammation caused by direct cell damage upon contact with a substance that is inherently harmful to cells [8]. Removal of the irritant is sufficient and the inflammation will resolve with time.

Erosions are characteristically described as delineated, moist, and depressed lesions resulting from disruption of a part or all of the epidermis [7]. Mild bleeding with pain or burning may also be present [9]. These changes may occur after trauma from the arrays, shaving injury, inflammation or maceration due to sweat, rupture of

Table 9.1 Potential causes of dermatologic adverse events (dAEs)

Adverse events	Potential cause	Intervention
Contact dermatitis	Allergy	Topical steroid
	• Tape	• Clobetasol
	• Hydrogel	• Betamethasone
	Chemical irritation	Array placement
	• Hydrogel	
Erosion and ulcers	• Moisture (sweat)	
	• Alcohol	
	Mechanical trauma	Array placement
	• Shaving	
	• Array pressure/removal	Topical antibiotics
Skin infections and pustules		• Mupirocin
	Array pressure leading to decreased perfusion	• Clindamycin
	Secondary bacterial infection	Topical or oral antibiotics
		• Cefadroxil
		• Mupirocin
		• Clindamycin

vesicles or bullae from infection, as well as epidermal necrosis. Typically, erosions do not result in scarring [7].

Ulcers represent a more severe form of dAEs in which loss of the epidermis and dermis has occurred, and therefore increasing the risk of scarring [7]. Ulcers may be necrotic or clean, and during the healing process may contain granulation tissue. As the ulcer heals, dried blood, serum, and exudate may form a crust [7]. Infection of the ulcerated skin is indicated by purulent, granular, or malodorous discharge.

With the abundance of microbes that exist on the skin, infection is common [10]. Pustules represent a purulent infection in the epidermis composed of leukocytes, cellular debris (yellow color), and bacteria (greenish-yellow color) [7]. White pus may represent sterile inflammatory reaction without the presence of microorganisms. Vesicles and bullae are fluid-filled lesions with clear content that may or may not be infected. They may arise from early viral infections or trauma by friction or shearing forces. When bullae are due to bacterial infection, they are called bullous impetigo [7].

Management of Dermatologic Adverse Events

Adverse events on the skin associated with TTFields therapy can be prophylactically prevented and intervened with specific treatments depending on the type of dAE. Prevention is preferred, but prompt recognition of dAEs is also important. Early signs that a dAE is developing may include erythema, edema, scaling, discharge, crusting, pain, pruritis, erosions, or any of the above in combination [7].

Prophylaxis is an important preventive measure that will preclude or limit adverse events on the skin. First and foremost, both patient and caregiver should be educated to recognize potential dAEs and, because they are the individuals preparing the scalp and exchanging the arrays, it is critical that they should have intimate knowledge about the skin integrity as well as appropriate training to apply and remove the arrays. The treating oncologist should also be available to manage these adverse events when they develop to ensure timely intervention.

Scalp preparation, if done correctly, will lower the risk of irritating the skin and also optimize the delivery of TTFields. Conditions on the scalp that can contribute to dAEs include hair length, moisture from sweat, existence of sebum, and the length of time the same set of arrays contact the skin. Modification of these conditions can lower the risk of dAEs. Access to the scalp requires removing arrays and thus proper scalp preparation is essential at each subsequent replacement of arrays.

Proper and timely shaving using an electric razor is recommended to maximize the closeness of the shave and to ensure array contact on the scalp. All effort to avoid cutting the skin should be taken and therefore a straight blade razor is not recommended. Once the skin has been compromised there is a concomitant increased risk of developing dAEs. To test the closeness of the shave, one can use gauze or a cotton ball soaked with 70% isopropyl alcohol and run it across the scalp. Detectable friction or resistance would indicate the need for a closer shave [7]. Furthermore, mineral oil should be applied before shaving because it allows for cleansing of the skin and facilitates the removal of bacteria and scale.

In order to adequately remove sebum from the scalp, fragrance-free shampoo should be used after shaving. Once rinsed, the scalp should be wiped with 70% isopropyl alcohol. By eliminating as much sebum as possible, the contact between arrays and scalp is enhanced.

Although each transducer array is stored in sterilized individual packages, other precautions to prevent infection are required. Prior to any exchange of the arrays, proper hand washing, sanitizing the electric razor, and cleaning of the scalp are recommended [7]. The use of 70% isopropyl alcohol will help sterilize the skin surface. In addition, the patient's electric razor should not be shared with other individuals.

Transducer array application and removal is a critical step in preventing dAEs. The layout takes into account the head size, tumor size, and tumor location in the patient. Although each array is placed according to the layout plan, avoiding sites of surgical scars and craniotomy closure hardware is important when placing the arrays. Skin breakdown, erosions, ulcerations, or any combination of dAEs may occur if the ceramic discs are applied over scars or hardware. The concurrent administration of anti-cancer agents such as temozolomide or bevacizumab may also impair normal skin turnover and wound healing, increasing the possibility of erosions or ulcerations.

During array re-application, which occurs approximately every 3 to 4 days, the position should be shifted approximately 0.75 inch (or 20 mm) from the prior location. In doing so, the hydrogel layer is re-positioned to an area between the prior contact sites [7]. Indentation of the surface of the scalp will indicate the last location

of the ceramic discs. Due to individual patient factors such as hyperhidrosis, some patients may require more frequent array changes. Less skin irritation will occur when arrays are removed carefully and without excessive force. Slow and even tension is recommended during removal, which takes approximately 60 seconds per array. If the arrays become difficult to remove, mineral oil can be applied directly to the scalp at the edges of the arrays to facilitate removal and to minimize the need to use excessive force. To avoid irritating the scalp, rubbing the skin to remove the remaining adhesives should be avoided and mineral oil should be applied to help dissolve the adhesive.

Patients and caregivers must be educated on proper scalp care during TTFields treatment. The hydrogel associated with the ceramic discs is hydrophilic, and may partially liquefy after physical activity or warmer weather due to increased sweating. Under these circumstances, changing the arrays on a more frequent basis, such as once every 1 to 2 days, may be necessary [7]. The risk of negative skin reactions and poor wound healing may increase when systemic medications are combined with TTFields therapy (see below). Likely culprits include prolonged use of corticosteroids, systemic chemotherapies, and targeted anti-cancer drugs.

Treatment interventions should be considered after a patient has developed dAEs. As defined by preclinical studies, the electric field frequency and intensity therapeutic parameters are preset into the device and cannot be modified. Therefore, this creates a predetermined “dose” that cannot be changed by the treating oncologist [7]. However, dAEs may be treated by pharmacological intervention, treatment interruption, or both. As discussed previously as a means of prophylactic intervention, relocating the arrays and avoiding the affected skin can also be used for treatment of established dAEs. For areas that cannot be avoided by simply shifting the arrays, sterile nonadherent dressing pads or gauzes can be inserted between ceramic discs and scalp surfaces with dAEs to temporarily avoid direct contact.

Pharmacological treatment primarily consists of topical therapies, such as corticosteroids and antibiotics. Dermatitis is primarily treated with topical corticosteroids. Since topical therapies can only be applied at the time of transducer array exchange, high-potency corticosteroid ointments or foams are recommended. When the epidermal barrier is compromised or signs of infection exist, topical antibiotics should be used. Skin flora on the scalp should designate the selected spectrum of antibiotics used. However, neomycin containing topical antibiotics should be avoided due to a high incidence of ACD in the general population.

Topical therapies should be applied and left for 15 to 30 minutes. Residue must be removed by either re-washing the scalp or by using 70 % isopropyl alcohol. Lipids in the creams and ointments may interfere with contact of the ceramic discs in the transducer arrays when residue remains on the skin. An alternative is the use of topical steroids and antibiotics that are delivered in a vehicle such as foam, which will dissolve within minutes after skin contact.

Treatment interruption and topical therapies may be required for patients suffering from intolerable dAEs. Discontinued array application for 2 to 7 days is frequently sufficient for the resolution of the dAEs in concordance with the cellular turnover rate in the epidermis [7]. However, the treating oncologist should recog-

nize that prolonged treatment interruption may compromise TTFields therapy efficacy as longer survival was noted among patients who had a compliance rate of $\geq 75\%$ when compared to those with $< 75\%$ compliance [3]. Given the likelihood of recurrence in glioblastoma patients, prophylactic measures to prevent dAEs are particularly important and should be used upon TTFields therapy re-application.

Dermatologic Adverse Events Associated with Combination Therapies

As TTFields therapy is approved for the treatment of glioblastoma, most patients have undergone or are still undergoing other forms of therapy. Frequently, patients will have healing scars from previous surgery. They may also be receiving concomitant systemic chemotherapy. Both situations complicate the use of transducer arrays, and should prompt the oncologist to monitor more frequent for severe dAEs. As each systemic chemotherapy or targeted drug therapy has its own unique adverse event profile, only treatments that are commonly used together with TTFields therapy will be discussed (Table 9.2).

Bevacizumab has been found to delay wound healing, including surgical wound closure [11, 12]. By inhibiting the vascular endothelial growth factor ligand, bevacizumab blocks angiogenesis, which is required for proper wound healing. Furthermore, the repetition of applying and removing transducer arrays, as well as shaving of the hair, from the scalp can expose the skin to frequent mechanical

Table 9.2 Preventive measures for TTFields combination therapy

Treatment	Mechanism of contribution to adverse event	Precautionary measures
Bevacizumab	Delayed wound healing	<ul style="list-style-type: none">• Avoid placing arrays at sites of surgical scars, recent surgical sites, sites of erosions/ulcerations• During manipulation of skin, take extra care to avoid compromising the skin barrier
Craniotomy	Inferior tensile strength of skin	<ul style="list-style-type: none">• Avoid placing arrays at sites of surgical scars, recent surgical sites
	Altered vascular supply to skin	
Temozolomide	Myelosuppression	<ul style="list-style-type: none">• Close monitoring for secondary infections• Close monitoring for bleeding• Close monitoring for rashes
Radiation	Radiation-induced cell death	<ul style="list-style-type: none">• Careful manipulation of skin at sites of radiation exposure

trauma [13, 14]. These factors combined with delayed wound healing will likely increase the frequency and severity of dAEs. Therefore, array placement at areas with compromised skin, such as previous surgical sites, must be avoided. When dAEs are detected, arrays must be placed in alternative areas. Furthermore, the oncologist caring for patients who are receiving concurrent bevacizumab needs to be aware of compromised wound healing, and extra care must be taken when manipulating their skin. Extra effort will also be needed to ensure proper prophylactic intervention in these patients to prevent significant morbidities associated with improper wound healing [15].

Temozolomide is a cytotoxic agent for glioblastoma patients and it has been found to cause neutropenia and thrombocytopenia [16]. If damage to the skin occurs during preparation or manipulation of the device, neutropenic or thrombocytopenic patients would be at a higher risk of developing secondary infections or severe bleeding, respectively. In addition, rashes have been reported in up to 4 % of patient's receiving temozolomide [17]. Monitoring these potential adverse events is critical given the increased susceptibility of these patients when using TTFields therapy concurrently. Although no studies to date have linked temozolomide to complications with wound healing, cell death induced by DNA alkylation [18] could potentially interfere with this process.

Radiation commonly compromises wound healing and can lead to atrophy of the skin, ulcer formation, and desquamation [19]. Up to 60 % of surgical patients who were previously treated with radiation experience complications [19]. Increased rates of infection and poor wound healing have been reported [16], likely resulting from death of skin cells and infiltration of immune cells at the site of radiation exposure. Patients with glioblastoma are typically treated with radiation to the head, leading to an increased likelihood of dAEs on the scalp when transducer arrays are applied. One must account for the repetitive mechanical forces that will be applied to the fragile, irradiated skin and adjust accordingly.

The initial recommended treatment of glioblastoma is surgical resection [20]. Thus, craniotomy scars will be present in the majority of patients. Scars that have not completely healed have inferior tensile strength and altered blood flow [11], and therefore they are more susceptible to developing dAEs. It is important to allow all scars to heal completely before array placement, and to refrain from placing arrays directly over these areas. In addition, proper post-operative wound care to surgical sites is highly recommended.

Patients with glioblastoma may also be treated with various combinations of anti-cancer therapies. As most patients will have undergone a craniotomy, treatment with bevacizumab in patients with craniotomy scars is common. Patients who have undergone a craniotomy and who are concomitantly treated with bevacizumab have been shown to have higher rates of wound healing complications post-operatively [15]. Therefore, with the application of transducer arrays and the use of TTFields therapy, applying proper prophylactic therapies and monitoring for dAEs are critical for these patients.

Conclusion

TTFields therapy is a novel anti-cancer treatment that involves physical contact of the transducer arrays with the scalp and has a unique profile of adverse events. The treating oncologist and other staff members must become familiar with these adverse events, and develop individualized plans for preventing and treating them. The continuous use of proper prophylactic measures, combined with the necessary treatment interventions when adverse events develop, are essential in managing patients on TTFields therapy. Moreover, the concurrent use of systemic agents, surgery or radiation may potentiate the frequency and severity of dAEs, requiring additional supportive care efforts, all of which will help to maintain QoL and maximize benefit from TTFields.

Quality of Life Issues in Patients Treated with Tumor Treating Fields Therapy

Tumor control and survival had traditionally been the primary focus of brain tumor treatment assessment. Clinical research was designed around clinical outcome parameters, which included primarily overall and progression-free survival as end-points. The emphasis was on extending life and less so on QoL. Although the concept of QoL in this context has been recognized for a long time, there has been a clear shift to more QoL-oriented medicine over the last 2 to 3 decades [21]. Functional performance has become another important assessment parameter of cancer patients after Karnofsky introduced a simple performance score, but an appreciation of its importance on survival and treatment response has led to a shift in what is considered therapeutic success in cancer clinical trials [22].

The assessment of QoL has therefore evolved into an important and fundamental part of oncologic trials as well as part of the routine protocol at clinical follow-up visits. QoL assessment consists of a number of domains that cover a multitude of aspects of performance and well-being, and tries to reflect the current social, economic, psychological, spiritual, and health status of the individual patient. Organ-specific QoL questionnaires for cancer patients have been designed and validated in order to characterize the disease-specific impact on an individual's life [23, 24]. In brain tumor patients—more than in other cancer patients—the disease affects multiple domains of well-being and performance. Patients often suffer from a multitude of neurological deficiencies and symptoms, seizures, and side effects from high-dose corticosteroids and anticonvulsive therapies, even before the initiation of prolonged radiation and chemotherapy [25].

The purpose of this section of the chapter is to summarize QoL issues related to the usage of TTFields therapy in patients with glioblastoma, a World Health Organization grade IV primary brain tumor and the most common primary malignant brain tumor affecting the adult population.

Quality of Life Assessment During Tumor Treating Fields Therapy

In contrast to conventional chemotherapies, biological therapies, and radiation treatment, TTFields therapy involves an externally applied device whose technical details [2, 4] and proposed mechanism of function have been described in depth elsewhere [26, 27]. Relevant for this review is the fact that continued treatment is applied through transducer arrays that are attached to the shaved scalp. These arrays are connected to a portable device that generates TTFields and, as such, affects tumor growth. This is the source of the main difference between its application to traditional drug treatments, and the reason why it might impact QoL in a different way. Scalp attached transducer arrays are connected and activated by the operating device for at least 18 hours a day in order to deliver effective treatment. As a result, patients and their families become closely involved in the provision of treatment and can take responsibility for its correct application on a daily basis.

Two phase III randomized clinical trials involving the application of the device in glioblastoma patients have thus far been conducted. The first trial (EF-11) compared TTFields monotherapy to Best Physician's Choice chemotherapy in glioblastoma patients with one or more recurrences. This trial included 120 patients randomized to the device arm, and the results were published elsewhere [2]. The second trial (EF-14) compared temozolomide maintenance therapy with and without TTFields therapy in over 700 newly diagnosed glioblastoma patients after completion of initial standard-of-care radiotherapy and concomitant daily temozolomide in multiple treatment centers. The results of the interim analysis on 315 analyzed patients were recently published [4] and the QoL-related results of both clinical trials are discussed here.

Outcome of Quality of Life Assessment

One of the important questions related to the use of the device in real life is patient compliance. The log file analyses that were generated by the device of patients treated in the EF-11 trial revealed a high mean compliance rate (86%, range 41–98%) that translated into a mean use of 20.6 hours per day. Completion of at least 1 month of treatment (i.e., a 4-week cycle) was documented in 79 out of 120 (65.8%) enrolled patients in the TTFields therapy arm. A *post hoc* subgroup analysis showed a trend towards better compliance and treatment efficacy [28].

There are no known systemic adverse events associated with the Optune® device, except for an occasional skin rash, itching, irritation or, in rare cases, skin ulceration. These adverse events are associated with the use of the scalp transducer arrays and defined as mild-to-moderate (grade 1 or 2) contact dermatitis, occurring in 16% of patients [2]. The dermatologic aspects of this therapeutic approach were presented in detail and discussed in the early part of this chapter.

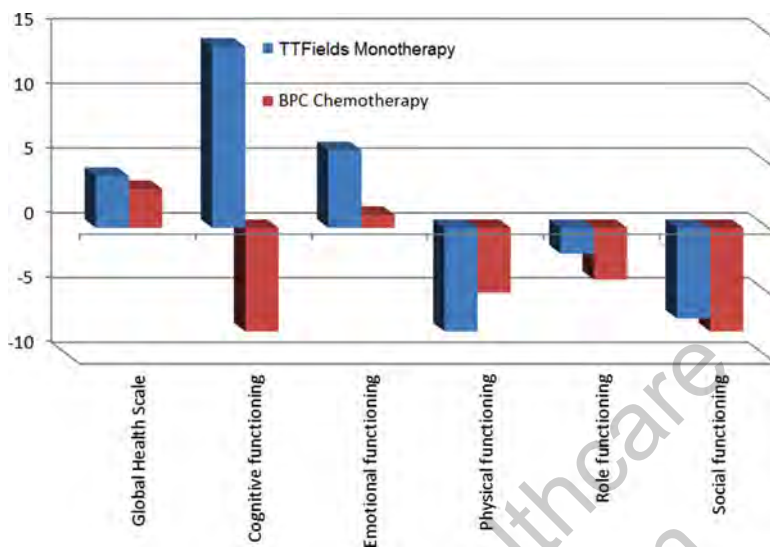


Fig. 9.1 Longitudinal change in QoL domains as recorded on the QLQ C-30 questionnaire from baseline to 3 months in the EF-11 trial. Change in % from baseline (negative values suggest worsening of the domain). *BPC* Best Physician's Choice, *QLQ* quality of life questionnaire, *QoL* quality of life

Participating patients in the EF-11 trial answered a standard QoL questionnaire (EORTC-QLQ C-30) [29] at the time of enrollment and every 3 months thereafter. A total of 63 (26 %) of those patients were available for a longitudinal QoL analysis (>3 months on study). Thirty-nine out of 120 (30 %) patients treated with TTFields monotherapy and 27 out of 117 (23 %) who received chemotherapy were eligible for a longitudinal QoL analysis. The QoL domains comprised a global health scale, as well as cognitive, emotional, physical, role and social functioning (Fig. 9.1). A striking difference was observed between the chemotherapy arm and the TTFields monotherapy arm in the domains of cognitive and emotional functioning, favoring the latter. There were no remarkable differences in global health, social, role, or physical functioning between the two treatment arms. In addition, treatment-associated toxicity was assessed by a symptom scale analysis (Fig. 9.2). As expected, appetite loss, constipation, diarrhea, nausea, and vomiting were predominantly associated with patients in the chemotherapy-treated arm. Pain and fatigue were reported only by patients in the chemotherapy arm and none in the TTFields-treated group.

The results of the EF-14 trial have only been published partially. The following are data of the interim analysis, after the completion of data collection on the first 315 randomized patients [4]. A total of 238 (75.6 %) patients who were enrolled in EF-14 were available for this longitudinal QoL analysis (>3 months into the study). Within this group, 171 out of 210 (81.4 %) received combined TTFields therapy and temozolomide and 67 out of 105 (63.8 %) treated with temozolomide only were eligible for this interim analysis. It should be borne in mind that both arms received standard temozolomide chemotherapy and that the study arm was additionally

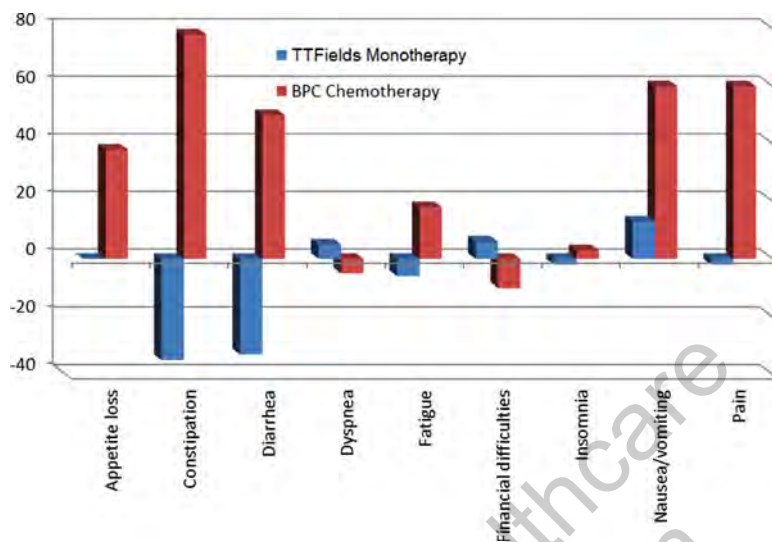


Fig. 9.2 Longitudinal change in symptom scale from baseline to 3 months in the EF-11 trial as recorded by a questionnaire. Change in % from baseline (negative values suggest improvement of symptoms). *BPC* Best Physician's Choice

treated with TTFields therapy. Chemotherapy-associated symptoms were more evenly distributed between the two study arms. In EF-14, the QoL domains were similar over a 9- to 12-month longitudinal observation period. A statistical analysis (two-way ANOVA) did not yield any meaningful differences yet.

Conclusions

Glioblastoma patients may have a number of treatment options at certain stages of their disease, and while the effectiveness of the various approaches might be quite similar, the therapeutic approach that has a superior QoL profile will be more appealing for the patient. As a result, a substantial portion of current cancer clinical trials is devoted to QoL issues. Patients with recurrent glioblastoma treated with TTFields monotherapy reported more favorable QoL outcomes and fewer adverse events compared to patients who were in the chemotherapy group in the EF-11 trial. However, in EF-14, chemotherapy-associated symptoms were more evenly distributed between the two study arms; the QoL domains were similar over a 9- to 12-month longitudinal observation period and there was no significant difference in any of the QoL domains. Taken together, TTFields monotherapy showed a more favorable QoL profile compared to chemotherapy alone, while TTFields in combination with chemotherapy did not impact the QoL of patients compared to chemotherapy alone.

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Chapter 10

Future Directions for Tumor Treating Fields

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Future evaluation of the efficacy of Tumor Treating Fields (TTFields) as delivered by the Optune® device will focus upon combination therapies for glioblastoma and monotherapy for other cancer types. Several clinical trials are being conducted and others are being planned for investigating use of TTFields in combination with stereotactic radiosurgery (SRS) and bevacizumab for glioblastoma, and as local treatment for non-small cell lung cancer brain metastasis, systemic lung cancer, mesothelioma, pancreatic cancer, and ovarian cancer. It is noteworthy that the testing of TTFields in humans started in neuro-oncology, initially for the treatment of recurrent glioblastomas (NCT00379470) [1] and later in newly diagnosed glioblastomas (NCT00916409) [2]. This route of development for a new anti-cancer therapy is highly unusual because treatments in neuro-oncology were traditionally adopted

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from established therapies from other disease sites, when the accompanying pre-clinical scientific data on the mechanisms of action have been firmly established. The two pivotal trials conducted in glioblastoma have helped to establish TTFields as a *bona fide* anti-cancer treatment that merits investigation in other types of malignancies outside the central nervous system. In this chapter, we will discuss current and emerging clinical trials that utilize TTFields alone or in combination with other modalities of treatment for glioblastoma and other central nervous system tumors (Table 10.1), and as monotherapy or combination therapy for systemic malignancies (Table 10.2).

Combination Treatments Using Tumor Treating Fields for Glioblastoma

The rationale for combining TTFields with SRS for recurrent glioblastoma is based on prior SRS trials that demonstrated a survival rate of 8 to 10 months [3–5]. Although not statistically comparable, especially because of significant differences in patient selection, survival after SRS appears favorable when compared to chemotherapy [6, 7]. Furthermore, from a radiobiological standpoint, large fraction radiotherapy might potentiate immune-mediated anti-tumor activity [8, 9]. The addition of TTFields after SRS may further potentiate this effect because tumor cells exposed to alternating electric fields exhibit cell surface expression of calreticulin and the secretion of HMGB1, both of which are required to generate immunogenic cell death [10–12]. In a retrospective analysis of patients with poor prognosis recurrent glioblastoma, the addition of SRS to TTFields therapy prolonged survival when compared to TTFields alone, with a median overall survival of 12 (95 % CI 4–20) months for SRS plus TTFields versus 4 (95 % CI 2–6) months for TTFields alone ($p=0.0036$), recognizing that different patients were selected for these treatment approaches [13]. Taken together, there is a biological rationale underpinning the combination of TTFields and SRS.

Bevacizumab is a humanized monoclonal antibody that inhibits the action of vascular endothelial growth factor and has been approved by the U.S. Food and Drug Administration for recurrent glioblastoma. It is another treatment modality that can be combined with TTFields in an effort to prolong the progression-free survival and/or overall survival of patients with recurrent glioblastoma. To date, clinical trials using single-agent bevacizumab for glioblastoma have not shown an improvement in overall survival but have demonstrated a benefit in progression-free survival [14, 15]. However, a *post hoc* analysis of the phase III EF-11 trial for recurrent glioblastoma revealed that the use of TTFields monotherapy among patients who had progressed on bevacizumab ($n=23$) resulted in an improved median overall survival of 6.0 months compared to those treated with chemotherapy ($n=21$) who had a median overall survival of 3.3 months (hazard ratio=0.43, 95 % CI, 0.22–0.85) [16]. Recurrent glioblastoma patients present a very difficult therapeutic challenge and an area of unmet need, and it is therefore hoped that the combination of TTFields and bevacizumab can potentially prolong their survival. In addition, the

Table 10.1 Clinical trials using TTFields in central nervous system malignancies.

Disease	Phase	Treatment	Endpoint	Status	NCT
Recurrent GBM	Pilot	TTFields + bevacizumab	PFS	Recruiting	NCT01894061
Recurrent GBM	II	TTFields + Bevacizumab	PFS	Recruiting	NCT02663271
Recurrent GBM	II	TTFields + genomic analysis to identify the genetic signature of response	ORR via RANO	Recruiting	NCT01954576
Recurrent GBM (first recurrence)	II	TTFields + bevacizumab/CCNU	AEs, PFS, OS	Pending	NCT02348255
Recurrent GBM (bevacizumab-naïve)	Pilot	TTFields + bevacizumab + SBRT	AEs	Recruiting	NCT01925573
Recurrent GBM	Pilot	TTFields	Response	Recruiting	NCT02441322
Newly diagnosed unresectable GBM	II	TTFields + bevacizumab + TMZ	AEs	Recruiting	NCT02343549
Recurrent atypical and anaplastic meningioma	Pilot	TTFields	PFS	Recruiting	NCT01892397
COMET: 1-5 NSCLC brain metastases (with controlled systemic disease)	II	TTFields vs. best supportive care	Time to cerebral and distant progression	Recruiting	NCT01755624
METIS: 1-10 NSCLC brain metastases	III	TTFields vs. best supportive care	Time to cerebral progression	Recruiting	NCT02831959

AEs adverse events, CCNU lomustine, GBM glioblastoma, NCT national clinical trial, NSCLC non-small cell lung cancer, ORR overall response rate, OS overall survival, PFS progression-free survival, RANO Response Assessment in Neuro-Oncology, SBRT stereotactic body radiation therapy, TTFields Tumor Treating Fields, TMZ temozolomide

Table 10.2 Clinical trials of TTFIELDS in extracranial solid tumor (non-central nervous system) malignancies.

Trial	Phase	Treatment	Endpoint	Status	NCT
PANOVA: Newly diagnosed advanced pancreatic	Open-label pilot	TTFIELDS + gemcitabine with/without nab-paclitaxel	AEs	Completed	NCT01971281
INNOVATE: Recurrent ovarian carcinoma	Open-label pilot	TTFIELDS + weekly paclitaxel	AEs	Completed	NCT02244502
STELLAR: Malignant pleural mesothelioma	II	TTFIELDS + pemetrexed + cisplatin/ carboplatin	OS	Recruiting	NCT02397928
LUNAR: Advanced non-small cell lung cancer	III	TTFIELDS + anti-PD1 inhibitor or paclitaxel	OS	Planning	Not available

AEs adverse events, NCT national clinical trial, OS overall survival, TTFIELDS Tumor Treating Fields

mechanism of action of TTFields is not limited by normalization of the blood brain barrier due to the use of concomitant bevacizumab as noted earlier. The favorable intracranial safety profile of TTFields and bevacizumab suggests that the combination will probably have an acceptable level of toxicity [16, 17]. There is a planned Radiation Therapy Oncology Group (RTOG) Foundation study on TTFields and bevacizumab in patients with recurrent glioblastoma that have progressed on bevacizumab. The primary endpoint is the overall survival rate at 6 months from registration, while the secondary endpoints include overall survival, progression-free survival, objective response rate, and the frequency of treatment-related adverse events.

There are a number of ongoing investigator-initiated trials combining TTFields and bevacizumab (Table 10.1). Two phase II studies are currently evaluating this combination in patients with recurrent glioblastoma (NCT01894061 and NCT02663271). Another investigator-initiated phase II trial is investigating TTFields therapy combined with bevacizumab and carmustine for the treatment of glioblastoma in first relapse (NCT02348255). A fourth study is evaluating the combination of TTFields with bevacizumab and hypofractionated stereotactic irradiation in bevacizumab-naïve patients with recurrent glioblastoma (NCT01925573); an important goal of this trial is to generate preliminary safety data for the concomitant use of fractionated radiation and TTFields. In addition, a phase II study on patients with newly diagnosed glioblastoma is evaluating the efficacy of combining TTFields with temozolomide and bevacizumab in the adjuvant phase of treatment, after initial radiotherapy with concomitant temozolomide and bevacizumab (NCT02343549). Collectively, these ongoing studies reflect the enthusiasm for multimodality combination therapy using TTFields plus other treatments such as bevacizumab and temozolomide, bevacizumab alone, or bevacizumab and radiosurgery or hypofractionated radiotherapy.

One important study is aimed at addressing the issue of finding genomic signatures that may correlate with the response to TTFields treatment in recurrent glioblastomas (NCT01954576). The subjects in the trial are stratified according to whether they are bevacizumab naïve or refractory, and the primary endpoint is overall response rate according to criteria established by Response Assessment in Neuro-Oncology (RANO) [18]. Another study utilizes high resolution magnetic resonance imaging and spectroscopy sequences, repeated at frequent intervals during TTFields treatment, to evaluate and potentially predict therapeutic response (NCT02441322). Together, these studies may offer important insights into the genomic background associated with radiologic response when patients are treated by TTFields.

Tumor Treating Fields for Brain Metastasis

TTFields are being investigated for the treatment of brain metastasis from non-small cell lung cancer. Preclinical experiments have demonstrated that multiple human lung cancer cell lines, including H1299 (adenocarcinoma), A549 (adenocarcinoma), HTB-182 (squamous cell carcinoma), and HCC827 (adenocarcinoma with mutated

Table 10.3 Summary of cell line-specific features in response to TTFields.

Cell line name	Tissue	Disease	Karyotype ^a	Optimal frequency (kHz)	Doubling time (h)
A2780	Ovary	Carcinoma	Modal chromosome number =46	200	18.7
A549	Lung	Adenocarcinoma	Hypotriploid, modal chromosome number =86 in 24 % of cells	150	23.8
AsPC-1	Pancreas	Adenocarcinoma	Not specified	150	54.0
HeLa	Cervix	Adenocarcinoma	Modal number =82; range = 70–164	150	24
MCF-7	Mammary gland: breast	Adenocarcinoma	Hypertriploidy to hypotetraploidy, modal chromosome number = 82	150	29.3
MDA-MB-231	Mammary gland: breast	Adenocarcinoma	Near-triploid, modal number =64	150	29.1
MSTO-211H	Lung	Biphasic mesothelioma	Modal chromosome number =72	150	26.4
NCI-H1299	Lung	Carcinoma; NSCLC	Not specified	150	23.1
NCI-H2052	Lung	Stage 4, mesothelioma	Not specified	200	18.9
U-87 MG	Brain	Grade IV glioblastoma: astrocytoma	Hypodiploid, modal chromosome number = 44 in 48 % of cells	200	34.0
U-118 MG	Brain	Grade IV glioblastoma: astrocytoma	Hypodiploid, modal chromosome number = 44 in 48 % of cells	200	18.5

From Giladi M. et al. Mitotic Spindle Disruption by Alternating Electric Fields Leads to Improper Chromosome Segregation and Mitotic Catastrophe in Cancer Cells. Scientific Reports. 5, 18046; doi: 10.1038/srep18046 (2015).

^aAccording to ATCC and/or NCI SKY/M-FISH and CGH Database

epidermal growth factor receptor [EGFR]), had maximal mitotic disruption at an electric field frequency of 150 kHz (Table 10.3) [19, 20]. There was also an additive effect *in vitro* on tumor cell killing when TTFields were combined with cytotoxic chemotherapies such as pemetrexed, cisplatin, and paclitaxel in H1299 and HTB182 cells, as well as targeted therapy such as erlotinib for the EGFR-mutated HCC827 cells [19]. Furthermore, using murine Lewis lung carcinoma cells and KLN205 squamous cell carcinoma cells orthotopically implanted into the left lung of C57BL/6 mice, *in vivo* efficacy was also observed when pemetrexed, paclitaxel, or cisplatin was combined with TTFields [19]. Therefore, there is a strong basis for the application of TTFields in human clinical trials because of its known anti-mitotic mechanisms of action, coupled with the observed robust anti-tumor activities *in vitro* and *in vivo*.

The COMET or EF-21 trial was designed to administer TTFields at a frequency of 150 kHz in a phase II randomized study conducted in Europe for non-small cell lung cancer brain metastasis (NCT01755624). Specifically, this trial enrolls patients with 1 to 5 newly diagnosed brain metastases treated initially with standard-of-care local therapy consisting of either SRS alone or surgery plus SRS, and then followed by randomization to receive TTFields therapy or supportive care. The primary endpoint is time to local or distant intracranial progression. Secondary endpoints include overall survival, 6-month intracranial disease control rate, neurocognitive function, quality of life, progression-free survival, and adverse events. A similar trial that is currently being implemented in the United States is the METIS or EF-25 trial (NCT02831959). The design is similar but METIS allows up to 10 brain metastases treated by local therapy and the analysis will be stratified according to the number of metastases [21].

Tumor Treating Fields for Atypical and Anaplastic Meningioma

Based on the emerging data on TTFields efficacy for recurrent and newly diagnosed glioblastomas, the Optune® device set at 200 kHz is being applied to other central nervous system tumors such as recurrent grade II atypical and grade III anaplastic meningiomas (NCT1892397). The trial is being conducted at multiple sites in the United States and approximately 21 subjects will be enrolled in the study. The primary outcome measure is progression-free survival and the secondary endpoints are overall survival as well as safety and tolerability.

Ongoing Studies of Tumor Treating Fields for Extracranial Solid Tumors

The effect of TTFields was also investigated preclinically in AsPC-1 and BxPC-2 human pancreatic adenocarcinoma cell lines, and the reported optimal frequency for anti-mitotic effects is 150 kHz [20, 22]. Interestingly, TTFields caused an increase in cell volume in both AsPC-1 and BxPC-2 cells, a finding consistent with

aberrant cytokinesis [20, 23]. These encouraging findings led to PANOVA, a double-arm, nonrandomized, open-label pilot trial, for advanced pancreatic carcinoma testing the safety of add-on TTFields to gemcitabine or to gemcitabine plus nab-paclitaxel (NCT01971281). This trial has completed patient accrual in Europe. Preliminary safety results from 20 enrolled subjects demonstrated 14 (70 %) had serious adverse events, of which 6 (30 %) were hematological, 9 (45 %) were gastrointestinal, and 3 (15 %) were pulmonary events [24]. There was 1 (5 %) fatality from intestinal perforation. Dermatitis, a known side effect of TTFields therapy, was reported in 10 (50 %) subjects and 2 (10 %) were grade 3 in severity but resolved with treatment. Six (30 %) had a partial response and another 6 (30 %) had stable disease. Therefore, the data available thus far indicate that treatment with TTFields in combination with gemcitabine or gemcitabine plus nab-paclitaxel has an acceptable safety profile and warrants further clinical trial investigation.

The optimal TTFields frequency for mitotic disruption is 200 kHz in A2780 ovarian carcinoma cells and *in vitro* experiments have shown a significant decrease in cellular viability and clonogenicity (by 45 % and 24 %, respectively) [20, 25]. *In vivo* mouse studies also showed activity with reduction in tumor luminescence by 40 % and tumor weight by 55 % [25]. These favorable preclinical data led to the development of a pilot phase I/II INNOVATE study of TTFields therapy at 200 kHz given in combination with weekly paclitaxel for recurrent ovarian carcinoma (NCT02244502). The primary endpoints are the adverse event rate and the number of patients prematurely discontinuing TTFields therapy due to skin toxicity. The secondary endpoints include progression-free survival, overall survival, 1-year survival rate, radiological response including duration of response, CA-125 biomarker response rate including response duration, and patient compliance. The study has completed accrual in Europe.

For mesothelioma cells, such as MSTO-211H and NCI-H2052, the optimal frequency for mitotic disruption is 150 kHz and 200 kHz, respectively [20]. Cell viability decreased by about 60 % in both cell lines and clonogenicity decreased by 70 % and 60 %, respectively [20]. A pilot study using the Optune® device at 200 kHz included a patient with pleural mesothelioma who experienced tumor regression near the site of TTFields application and stabilization of other distally located tumors [26]. The phase II STELLAR trial is now testing the efficacy of TTFields in combination with cisplatin or carboplatin for malignant pleural mesothelioma (NCT02397928). The primary endpoint is overall survival, and the secondary endpoints are progression-free survival, response rate, and adverse event rate. This study is being conducted at multiple sites in Europe and is expected to enroll 80 subjects.

Non-small cell lung carcinoma cells, such as H1299 and A549, are disrupted by TTFields at 150 kHz frequency. In particular, A549 cells exhibited marked mitotic spindle disruption upon exposure to TTFields [20]. Based on the preclinical data, the LUNAR or EF-24 trial will be conducted as a randomized study to investigate the benefit of TTFields at the 150 kHz frequency when added to anti-PD1 checkpoint inhibitor therapy or paclitaxel for patients with advanced non-small cell carcinoma

of the lung. The primary objective is overall survival and secondary objectives include progression-free survival, radiological response, and quality of life assessment. This study is being planned to enroll subjects in the United States and Europe.

Conclusions

Future directions for the treatment of glioblastoma by TTFields will involve combination therapies when TTFields are added onto existing regimens or combined with personalized medicine based on genomic profiling. These combinations may include SRS, hypofractionated radiation, bevacizumab, and/or cytotoxic chemotherapy, such as temozolomide or lomustine. Furthermore, a number of trials for the treatment of central nervous system tumors other than glioblastoma have been initiated since 2012, including investigator-initiated trials for recurrent atypical and anaplastic meningiomas. There are ongoing or planned studies for brain metastases from non-small cell lung cancer as well. Lastly, TTFields efficacy is also being studied for the treatment of extracranial solid tumor malignancies, such as pancreatic adenocarcinoma, ovarian carcinoma, pleural mesothelioma, and non-small cell lung carcinoma. As these trial results accumulate over time, TTFields may potentially become an efficacious treatment modality that can be applied to multiple types of malignancies.

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NOVOCURE LIST OF PATENTS
July, 2018

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7016725	Method and Apparatus for Destroying Dividing Cells
7089054	Apparatus and Method for Treating a Tumor or the Like
7136699	Apparatus for Destroying Dividing Cells
7146210	Apparatus and Method for Optimizing Tumor Treatment Efficiency by Electric Fields
7333852	Method and Apparatus for Destroying Dividing Cells
RE43618	Method and Apparatus for Destroying Dividing Cells
7467011	Hat for Treating a Tumor or the Like
7519420	Apparatus for Selectively Destroying Dividing Cells
7565205	Treating a Tumor or the Like with Electric Fields at Different Orientations
7565206	Treating a Tumor or the Like with Electric Fields at Different Orientations
7599745	Treating a Tumor or the Like with an Electric Field
7599746	Apparatus and Method for Preventing the Spread of Cancerous Metastases and for Elimination of Metastases
7706890	Treating a Tumor or the Like with an Electric Field that is Focused at a Target Region
7715921	Electrodes for Applying an Electric Field In-Vivo Over an Extended Period of Time
7805201	Treating a Tumor or the Like with an Electric Field
7890183	Treating Parasites with Electric Fields
7912540	Article of Clothing for Treating a Tumor or the Like
7917227	Optimizing Characteristics of an Electric Field to Increase the Field Effect on Proliferating Cells
8019414	Treating Cancer Using Electromagnetic Fields in Combination with Other Treatment Regimens
8027738	Probe for Treating a Tumor or the Like
8170684	Electrodes for Applying an Electric Field In-Vivo Over an Extended Period of Time
8175698	Treating Bacteria with Electric Fields
8229555	Probe for Treating a Tumor or the Like
8244345	Treating a Tumor or the Like with Electric Fields at Different Frequencies
8406870	Treating Cancer Using Electromagnetic Fields in Combination with Other Treatment Regimens
8447395	Treating Bacteria with Electric Fields
8447396	Treating Bacteria with Electric Fields
8465533	Treating Cancer Using Electromagnetic Fields in Combination with Photodynamic Therapy
8706261	Treating a Tumor or the Like with Electric Fields at Different Frequencies
8715203	Composite Electrode
8718756	Optimizing Characteristics of an Electric Field to Increase the Field's Effect on Proliferating Cells
8764675	Composite Electrode
9023090	Treating Cancer Using Electromagnetic Fields in Combination with Photodynamic Therapy
9023091	Treating Cancer Using Electromagnetic Fields in Combination with Photodynamic Therapy

9039674 Treating Bacteria with Electric Fields
9056203 Treating Bacteria with Electric Fields
9440068 Treating Bacteria with Electric Fields
Optimizing Treatment Using TTFields by Changing the Frequency During the Course of Long
9655669 Term Tumor Treatment
9750934 Treating Bacteria with Electric Fields
High Voltage, High Efficiency Sine Wave Generator with Pre-Set Frequency and Adjustable
9910453 Amplitude

DRAFT



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Arlington, Virginia

Appellant:

ALJ Appeal No.: 1-7585537269

Enrollee:

Medicare: Part C

HICN:

Before: Scott Anderson
Administrative Law Judge

DECISION

After carefully considering the evidence in the record and arguments presented at the hearing, I enter a **FULLY FAVORABLE** decision for the Appellant/Enrollee (Appellant) in this matter.

PROCEDURAL HISTORY

Appellant is enrolled in HumanaChoice a Medicare Advantage Plan administered by Humana (hereinafter Humana or the Plan). Appellant submitted a claim to the Plan for pre-approval of an electrical stimulation device used for cancer treatment (HCPCS E0766) to be provided by the Provider, Novocure, Inc. (also known as Optune) from March 30, 2018 to September 30, 2018. On April 10, 2018, Humana denied the request because:

Your condition did not meet the Medicare rule for approval of a device used for cancer treatment (electrical stimulation device used for cancer treatment includes all accessories, any type). Your records show you have brain cancer (malignant neoplasm of brain). The Medicare rule says tumor treatment field therapy will be denied as not reasonable and necessary. Under Medicare rules your request is not medically necessary.

Ex. 1 at 24.

In a May 7, 2018 letter, treating oncologist
Appellant's behalf. Ex. 1 at 33-34. The requested stated:

M.D., requested redetermination on

[Appellant] sought medical treatment and was found to have a right frontal brain mass. She underwent a gross total resection on December 4, 2017 which was followed by courses of radiation and Temozolomide. As of March 22, 2018 her neurological deficits have all resolved, however, post-operative MRI on the same date was documented as concerning for recurrent neoplasm. Suspicion is so high that [Appellant] was planned for a follow-up MRI at a one month interval as opposed to a 2 month interval.

After discussing treatment options with [Appellant], I have decided to prescribe Optune in combination with [T]emozolomide as this currently is the best option for treating her glioblastoma.

Alternative electric field therapy (Optune) + adjuvant temozolomide is now an NCCN Category 2A recommendation following postoperative standard brain radiation therapy with concurrent [T]emozolomide.

...

Optune received pre-market approval from the FDA for recurrent glioblastoma in April 2011. This approval was based on the results of a large randomized controlled trial of patients with recurrent GBM comparing Optune as a monotherapy to standard chemotherapy use in recurrent GBM. The results showed that treatment with Optune delivered comparable overall survival and progression free survival to chemotherapy with minimal toxicity and an improvement in patients quality of life compared to chemotherapy.

In 2015, Optune received pre-marketing approval from the FDA for newly diagnosed glioblastoma in combination with [T]emozolomide after standard surgical resection and radiation therapy.

...

It is my belief that Optune in combination with [T]emozolomide is the most appropriate option for [Appellant] at the present time.

Ex. 1 at 33-34 (emphasis in original).

In response, Humana upheld the initial determination, stating that: "Local Coverage Determination (LCD) for Tumor Treatment Field Therapy (TTFT) (L34823) for Indiana, which states, 'T field therapy (E0766) will be denied as not reasonable and necessary.'" Ex. 1 at 15.

Appellant requested reconsideration from Maximus Federal Services (MAXIMUS), a Medicare Independent Review Entity (IRE). In an unfavorable decision dated May 24, 2018, the IRE denied coverage on the basis that the medical records did not meet the requirements of Local Coverage Determination (LCD) L34823. Ex. 1 at 3-4.

Appellant timely requested a hearing before an Administrative Law Judge to review that IRE's denial of Medicare Part C benefits. Ex. 3. The amount in controversy meets the jurisdictional amount; therefore, there is jurisdiction to hear and decide this case.

I conducted a hearing by telephone on September 5, 2018. At the hearing, Appellant's interest was represented by Novocure, the Provider, which was in turn represented by Stephanie Hales, Esq. Also appearing for the Provider were Dan McCoy, and Julie Miles, RN (Clinical Specialist), and the Appellant's husband. Humana appeared at the hearing through its representative Marcia Taylor and its witness Bryan Carr, M.D. Elizabeth Lemester, M.D., from Humana observed the hearing, but did not testify or participate. I administered oaths to Mr. McCoy, Ms. Miles, Mr. Ms. Taylor and Dr. Carr. Ms. Miles, Mr. and Dr. Carr testified at the hearing. I admitted Exhibits 1-5 into the record. During the hearing I heard testimony concerning recent medical test results and asked Appellant to submit that documentation so the record was complete. Humana had no objection. Having received that documentation shortly after the hearing, I now admit it as part of Exhibit 4.

ISSUE

Whether Humana is required to cover an electrical stimulation device used for cancer treatment (HCPCS E0766) provided to the Appellant?

FINDINGS OF FACT

1. The Appellant is a 75 year-old female who has the diagnosis of right frontal glioblastoma. Ex. 2 at 6.
2. On December 4, 2017, the Appellant had a gross total resection of the lesion and a specimen was biopsied. Ex. 2 at 6, 9, 12.
3. From January 18, 2018 to February 26, 2018, Appellant received the following treatments: "Temozolomide and XRT – total dose to the tumor bed to 5940 cGy." Ex. 2 at 6.
4. In a March 29, 2018 progress note the impression of M.D., was "[i]ncreased perfusion, nodular enhancement, and focal diffusion restriction in the posterior superior margin of the resection cavity is concerning for residual and recurrent neoplasm." Ex. 2 at 8; *see also* Ex. 2 at 18.

5. Dr. [redacted] provided Adjuvant Temozolomide/Optune TTF on May 3, 2018. Dr. [redacted] assessment was that Appellant "has evidence of disease progression on the imaging. This is not confined to previously irradiated areas, so I do not believe that it is pseudo progression. She is very early in her therapy in the adjuvant setting, and it is very concerning. . . . The question is really whether or not her current therapy (adjuvant temozolomide and TTF) has had sufficient treatment time to assess it is progressive." Ex. 2 at 2.
6. An August 20, 2018 MRI of Appellant's brain showed that "[t]here has been interval reduction of the confluent T2/FLAIR signal in the right frontal lobe, compatible with decreased surrounding vasogenic edema." Ex. 4.

LEGAL FRAMEWORK

A. Jurisdiction

An individual or organization that is dissatisfied with a reconsideration of a Contractor's initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (Secretary) provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act § 1869(b)(1)(A). The Secretary administers the nationwide hearings and appeals system through the Office of Medicare Hearings and Appeals (OMHA). Administrative Law Judges (ALJs) within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council.

A request for hearing meets the amount in controversy requirement if it comports with 42 C.F.R. § 405.1006(b)(1). A request for hearing is timely if filed within sixty days after receipt of the notice of the Qualified Independent Contractor decision. 42 C.F.R. § 405.1002(a)(1).

B. Scope of Review

"The issues before the administrative law judge include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in [the appellant's] favor. However, if evidence presented before or during the hearing causes the administrative law judge to question a fully favorable determination, he or she will notify [the appellant] and will consider it an issue at the hearing." 42 C.F.R. § 405.1032(a).

The ALJ may decide a case on the record and not conduct an oral hearing if the decision is fully favorable, or if the appellant indicates in writing that he does not wish to appear before the ALJ at a hearing. 42 C.F.R. § 405.1038.

C. Standard of Review

"The ALJ conducts a de novo review and issues a decision based on the hearing record." 42 C.F.R. § 405.1000(d).

Principles of Law

A. Statutes and Regulations

According to § 1862(a)(1)(A) of the Social Security Act ("Act"), Medicare may not make a payment under part A or part B for anything which is not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. (*See also* 42 C.F.R. § 405.860). However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that establishes criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (LCDs). Administrative Law Judges are not bound by LCDs, but will give substantial deference to these policies when applicable. (42 C.F.R. § 405.1062). If an Administrative Law Judge does not follow a policy in a particular case, the Administrative Law Judge must explain why in the decision. (42 C.F.R. § 405.1062).

CMS Medicare Managed Care Manual (MMCM), 100-16, Ch. 40 sets forth specific guidance regarding Medicare cost plans.

Although not subject to the force and effect of law, CMS and its contractors issue policies, manuals and guidelines that describe criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (LCDs). 42 C.F.R. § 405.1062 states that an ALJ is not bound by LCDs or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect.

LCD L34823 entitled "Tumor Treatment Field Therapy (TTFT)" provides that TTFT (E0766) will be denied as not reasonable and necessary.

The undersigned notes that the LCD contains a blanket citation to authorities for support but provides no rationale, discussion or criteria upon which exceptions can be made within the context of the LCD, or upon which the LCD is based. Moreover, it does not discuss what authorities it specifically relies upon, nor what the authorities purport to state.

Policy Article A52711 provides additional guidance for TIFT, and seems to provide some inconsistent analysis with the LCD, as follows:

NON-MEDICAL NECESSITY COVERAGE AND PAYMENT RULES:

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed- body member, and 3) meet all other applicable Medicare statutory and regulatory requirements.

Information provided in this policy article relates to determinations other than those based on Social Security Act §1862(a)(1)(A) provisions (i.e. "reasonable and necessary"). Tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act §1861(s)(6)). In order for a beneficiary's equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met. In addition, there are specific statutory payment policy requirements, discussed below, that also must be met.

Code E0766 is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling.

The accompanying Policy Article establishes that TTFT is categorized under the Durable Medical Equipment benefit. The article explains that code E0766 describes "devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers." The article further states that TTFT devices are in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. While it defers to any applicable LCD it seems to confirm categorically that in particular cases such treatments should be found to be medically reasonable and necessary. Additionally, it anticipates that any applicable LCD will provide eligibility criteria.

C. Evidence of Coverage

The Plan at issue is a Medicare Advantage Plan. The Plan's EOC states that as a Medicare health plan, the plan "must cover all services covered by Original Medicare and must follow Original Medicare's coverage rules." Ex. 5 at 43. Covered services include "all the medical care, health care services, supplies, and equipment that are covered by our plan." *Id.*

ANALYSIS

After careful consideration of the evidence and arguments presented, I conclude that the Novocure/Optune treatment is reasonable and necessary for purposes of coverage under Medicare Part C for the Appellant.

An MA plan must provide an enrollee with coverage for all items and services covered by Medicare Part A (except hospice services) and Part B that are available to beneficiaries in the plan's service area. See Section 1852 (a) (1) of the Social Security Act (Act); 42 C.F.R. §§422.100. An MA plan must comply with National Coverage Determinations (NCDs), general coverage guidelines included in original Medicare manuals and instructions, and written coverage decisions of local Medicare contractors with jurisdiction over claims in the geographic area in which services are covered under the MA plan. Therefore, if Medicare does not cover an item or service, unless the plan covers the item or service through supplemental benefits, the Plan is not required to cover the item or service at issue. See 42 C.F.R. § 422.102.

An LCD is program guidance developed by a Medicare contractor and is applicable only in that contractor's service area. An ALJ is not bound by program guidance such as LCDs, program memoranda, or manual instructions. However, an ALJ must give such policies substantial deference if applicable in a particular case. 42 C.F.R. § 405.1062(a). If an ALJ declines to follow a policy in a particular case, the rationale for not following that policy must be explained. 42 C.F.R. § 405.1062(b).

At the hearing Ms. Hales discussed that the Appellant's claim for coverage was denied by Humana and the Part C IRE based on Humana's reliance on the LCD. Hearing Record. Ms. Hales argued that TTFT treatment should be available for Appellant because a departure from the LDC is appropriate here. *Id.* Mr. Hales argued that the plan was required to follow the LCD, but noted that the ALJ has the discretion to decline to follow the policy put forth in an LCD. *Id.* Ms. Hales stated that Appellant has a particularly aggressive cancer and that there are limited treatment options. She stated that there is a broad medical consensus related to TTFT. In regard to Appellant, she started the treatment while this appeals have been pending and she has been well while on the therapy. Appellant would like to continue the therapy. She argued that Appellant's physician is an expert related to this treatment and that the physician stated in the requested for expedited review that TTFT was necessary, which aligns with FDA recommendations. Ms. Hales said that most insurance now covers TTFT. Ms. Hales said that specific to Ms. Haas that she is a good candidate for the TTFT, and that she has tolerated it and has been doing well. Ms. Hales argued that Departure from the LCD should be allowed based on the totality of the circumstances.

Julie Miles, RN, testified regarding the Appellant's symptoms and diagnosis which was glioblastoma, a very aggressive and rare form of brain cancer. *Id.* Ms. Miles testified that in December 2017, Appellant had a gross resection of the tumor and radiation. In March, there was concern of progression and TTFT was approved by the physician since treatment through surgery and radiation had already occurred. By July 2018, the situation had stabilized.

Ms. Miles discussed the recent acceptance by the FDA of TTFT treatment for newly diagnosed and reoccurrences of glioblastoma. *Id.* Ms. Miles also discussed recent studies and positive trials and noted that one study was even aborted mid-stream when it was discovered that the TTFT was so effective, it was determined to be unfair to continue to deny the treatment to the patients in the placebo group. *Id.* Mr. Hales also testified that the NCCN is the recommended compendia for providers of cancer treatments and noted the favorable treatment of TTFT in the NCCN and multiple published articles and journals. Ms. Miles concluded by testifying regarding the benefits of TTFT and how it has impacted the glioblastoma universe through statistically significant improvement in survival rates. *Id.*

Appellant's husband, testified that Appellant has been on TTFT and that Appellant has had no growth in the cancer and was stable. He stated that he would prefer for Appellant to stay on TTFT.

Bryan Carr, M.D., testified that Medicare Advantage Plans have to follow LCDs and that in this case, TTFT is not medically reasonable and necessary under the applicable LCD.

I agree with Appellant's counsel that the totality of the circumstances in this case support a departure from strictly following the LCD applicable to this case. Appellant initially received surgery and radiation to treat the diagnosed glioblastoma. However, an MRI showed progression of the disease and Appellant's physician determined that TTFT was the most appropriate treatment for the aggressive cancer that Appellant has, which was undeterred following conventional treatments. Ex. 1 at 33-34. The LCD does not explain why it categorically concludes that TTFT is not medically reasonable and necessary; however, the FDA and NCCN provide considered views that TTFT might well be reasonable and necessary as ordered by Appellant's oncologist after surgery and radiation. It is important to note that I do not attempt here to invalidate LCD 34823. Indeed I have no such authority. 42 C.F.R. § 405.1062(c). Rather, looking at the medical facts in this case along with updated medical views of the efficacy of TTFT, it appears that the categorical prohibition LCD 34823 states for TTFT is not warranted in Appellant's particular case. Because LCD 34823 provides no explanation for its approach to TTFT, I cannot conclude, based on the record before me, that TTFT is not medically reasonable and necessary for Appellant.

CONCLUSION OF LAW

1. Based on the totality of evidence of record, I conclude that Tumor Treatment Field Therapy is medically reasonable and necessary for Appellant under Title XVIII of the Social Security Act, Medicare Part C, Medicare Guidelines, and the terms of the health plan.
2. Humana is required to grant Appellant's approval request for the TTFT.

ORDER

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

SEP 19 2018

Dated: _____



Scott Anderson
Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Cleveland Field Office
Cleveland, Ohio

Appeal of:

[REDACTED]

ALJ Appeal No.: 1-7477540343

Beneficiary:

[REDACTED]

Medicare Part: C

HICN:

*****3949A

Before: John M. Bergen
U.S. Administrative Law Judge

DECISION

This is an appeal before me on a timely request for hearing filed by [REDACTED] ("Appellant"). I have carefully considered all of the applicable law, regulations, written guidelines, testimony and argument at the hearing, and documentary evidence in the record. For the reasons discussed below, I enter a FAVORABLE decision for the Appellant.

PROCEDURAL HISTORY

The initial request by the Appellant for tumor treatment field therapy (HCPCS code E0776) was denied. The Appellant requested a redetermination, and the Appellant's Medicare Advantage Plan, Independent Health's Medicare Passport (PPO) ("Plan") issued an unfavorable decision against the Appellant. Maximus Federal Services, a Qualified Independent Contractor ("QIC"), conducted a reconsideration and decided unfavorably against the Appellant.

Appellant timely filed an appeal and request for an Administrative Law Judge ("ALJ") Hearing, pursuant to 42 C.F.R. § 405.1002(a), which was received by the Cleveland, Ohio, office of OMHA. The amount in controversy meets the jurisdictional requirements for a hearing at OMHA.

A hearing was held on 5/29/18 at 1:00pm EST via teleconference originating from the Cleveland, Ohio, regional office of the Office of Medicare Hearings and Appeals. Appearing at the hearing was the Appellant. Stephanie Hale, attorney, Justin Kelly, RN, Dr. Ajay Abad, MD, Dr. Caroline Farrell, also appeared on behalf of the Appellant. Sarah Shuster, attorney, Dr. Michael Merrill, MD, and Darlene Feskun, RN,

appeared on behalf of the Plan. The exhibits were entered into the record without objection.

On 6/1/18 the Appellant submitted documents which were not included in the record for the previous decisions. Such documents are found in Exhibit 4 of the record. 42 C.F.R. § 405.1018 (c) states any evidence submitted by a provider, supplier, or beneficiary represented by a provider or supplier that is not submitted prior to the issuance of the QIC's reconsideration determination must be accompanied by a statement explaining why the evidence was not previously submitted. Pursuant to 42 C.F.R. §§ 405.1018 and 405.1028 the undersigned finds that the Appellant's letter which accompanied the evidence shows good cause as to why the evidence was not submitted previously and I hereby admit such evidence.

ISSUE

Whether the tumor treatment field therapy (HCPCS code E0776) requested by the Appellant must be covered by the Plan.

FINDINGS OF FACT

The following facts were established by a preponderance of the evidence:

The Appellant is 70 years old and is a member of the Plan. The Appellant suffers from glioblastoma. Ex. 3 at 14.

The Appellant underwent a craniotomy to excise his glioblastoma on 11/29/17. Ex. 3 at 14. Postoperatively, he received chemotherapy and radiation therapy to treat his glioblastoma. *Id.*

On 2/2/18 the Appellant's nurse practitioner, Kathleen Mogensen, NP, requested a six month rental of an Optune device and Transducer Arrays for the Appellant. Ex. 3 at 11. Optune is a wearable, portable, FDA-approved device indicated to treat a type of brain cancer called glioblastoma multiforme (GBM) in adult patients 22 years of age or older.¹

Dr. Abad, a neuro-oncologist, testified the Appellant's disease was found to be a very aggressive, grade IV, tumor. Hearing Testimony. The Appellant has received Temozolomide, radiation therapy, and a vaccine in addition to tumor treatment field therapy. Hearing Testimony. The molecular composition of the Appellant's cancer is less amenable to the effects of his Temozolomide than other glioblastoma tumors. Hearing Testimony. He also testified that for several years the prognosis of someone with the Appellant's condition was between 14 and 15 months, but tumor treatment field therapy is the first new therapy in years to improve a patient's prognosis. *Id.* Dr. Abad also testified that tumor treatment field therapy in addition to Temozolomide is best course of treatment a patient with glioblastoma can undergo. *Id.*

¹ <https://www.optune.com/therapy/optune-at-first-glance> (last visited 5/21/18)

The Appellant submitted several peer reviewed studies which described the efficacy of tumor treatment field therapy, including Roger Supp, MD, et. al., *Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma*, Vol. 314 JAMA Number 23 (2015). The conclusion of study was that tumor treatment field therapy with Temozolomide significantly prolonged progression-free and overall survival of patients with glioblastoma. Ex. 3 at 45.

LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act (Act) § 1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. See 70 Fed. Reg. 36386, 36387 (June 23, 2005), as amended by 76 Fed. Reg. 19995 (August 8, 2011). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

A hearing before an ALJ is only available if the remaining amount in controversy is one hundred sixty dollars (\$160) or more. See 82 Fed. Reg. 45592 (Sep. 29, 2017); 42 C.F.R. § 405.1006. The request for hearing is timely if filed within sixty (60) days after receipt of a QIC reconsideration decision. 42 C.F.R. § 405.1014(b)(1).

These appeals are before the ALJ on a timely request for hearing. The amounts in controversy meet the jurisdictional requirements for an ALJ hearing before OMHA. 42 C.F.R. § 405.1006; 82 Fed. Reg. 45592 (Sep. 29, 2017).

B. Scope of Review

The Centers for Medicare and Medicaid Services ("CMS") promulgated regulations implementing the Medicare, Medicaid, SCHIP Benefits Improvement and Protection Act of 2000, Pub. Law 106-554, app. F, 114 Stat. 2763, 2763A-463 ("BIPA"), and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. Law 108-173, 117 Stat. 2066 ("MMA"). Accordingly, all initial determinations subsequent to January 1, 2006, and all cases subject to a QIC reconsideration, are governed by the ALJ hearing procedures outlined in 42 C.F.R. §§ 405.900 through

405.1064. See 70 Fed. Reg. 11420, 11424-26 (Mar. 8, 2005), as amended by 70 Fed. Reg. 37700 (June 30, 2005), 70 Fed. Reg. 50214 (August 26, 2005), and 74 Fed. Reg. 65296 (December 9, 2009).

The issues before the ALJ include all the issues brought out in the initial determination, redetermination or the reconsideration, that were not decided entirely in the Appellant's favor. 42 C.F.R. § 405.1032 (a). However, if evidence presented before the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. *Id.* at § 405.1032 (b).

The ALJ may decide a case on the record and decline to conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing or the evidence in the hearing record supports a finding in favor of the Appellant on every issue. *Id.* at § 405.1038.

C. Standard of Review

The ALJ is not bound by the proceedings below. Instead the regulations call for a *de novo* review, resulting in a decision by the ALJ based on the hearing record. *Id.* at § 405.1000(d); *In the Case of Atlantic Anesthesia Associates, PC*, MAC (June 17, 2004) ("[A]n ALJ qualified and appointed pursuant to the Administrative Procedure Act acts as an independent finder of fact in conducting a hearing pursuant to section 1869 of the [Social Security] Act. This requires *de novo* consideration of the facts and law.").

II. Principles of Law

The Medicare program, Title XVIII of the Act, is administered through the Centers for Medicare and Medicaid Services, a component of the HHS.

Under Medicare Part C, A Medicare Advantage Plan must pay for those items and services (other than hospice benefits) for which benefits are available under Part A and Part B. 42 C.F.R. § 422.101 (2005) and Title XVIII, Social Security Act, § 1852. A Medicare Advantage Plan can provide additional health care items and services that are not covered under Part A and Part B. 42 C.F.R. § 422.101 (2005) and Title XVIII, Social Security Act, § 1852. A Medicare Advantage Plan must provide plan enrollees with coverage of the basic benefits they are entitled to by "furnishing those benefits directly or through arrangements, or by paying for the benefits." 42 C.F.R. § 422.100 (2005).

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program unless it is promulgated as a regulation by CMS. However, although not subject to the force and effect of the law, CMS and its contractors, have issued policy and guidelines that describe criteria for coverage for selected types of medical services and supplies.

Section 1861 of the Act provides that "medical and other health services" for which payment may be made under Medicare include durable medical equipment:

(s) The term "medical and other health services" means any of the following items or services:

(6) durable medical equipment;

Moreover, while not specifically stated, durable medical equipment, as defined in § 1861 of the Act, includes devices for home use:

(n) The term "durable medical equipment" includes iron lungs, oxygen tents, hospital beds, and wheelchairs (which may include a power-operated vehicle that may be appropriately used as a wheelchair, but only where the use of such a vehicle is determined to be necessary on the basis of the individual's medical and physical condition and the vehicle meets such safety requirements as the Secretary may prescribe) used in the patient's home (including an institution used as his home other than an institution that meets the requirements of subsection (e)(1) of this section or section 1819(a)(1)), whether furnished on a rental basis or purchased, and includes blood-testing strips and blood glucose monitors for individuals with diabetes without regard to whether the individual has Type I or Type II diabetes or to the individual's use of insulin (as determined under standards established by the Secretary in consultation with the appropriate organizations); except that such term does not include such equipment furnished by a supplier who has used, for the demonstration and use of specific equipment, an individual who has not met such minimum training standards as the Secretary may establish with respect to the demonstration and use of such specific equipment.

See also 42 C.F.R. § 410.36.

A further requirement under § 1862(a) of the Act provides, in pertinent part:

Notwithstanding any other provision of this title, no payment may be made under Part A or Part B for any expenses incurred for items or services--

(1)(A) which, except for items and services described in a succeeding subparagraph, are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

See also 42 CFR 411.15(k)(1).

B. Manuals

Although not binding on the Administrative Law Judge, manuals issued by CMS provide guidance in the administration of the Medicare program. In *Shalala v. Guernsey Memorial Hospital*, 514 U.S. 87, 102 (1995), the United States Supreme Court concluded an agency manual section is a valid interpretive rule and it is reasonable for the agency to follow it. Applicable in this case, MPIM ch. 5, § 5.7 provides the Medicare

guidelines regarding documentation requirements for DMEPOS. Specifically, the manual states:

For any DMEPOS item to be covered by Medicare, the patient's medical record must contain sufficient documentation of the patient's medical condition to substantiate the necessity for the type and quantity of items ordered and for the frequency of use or replacement (if applicable). The information should include the patient's diagnosis and other pertinent information including, but not limited to, duration of the patient's condition, clinical course (worsening or improvement), prognosis, nature and extent of functional limitations, other therapeutic interventions and results, past experience with related items, etc. If an item requires a CMN or DIF, it is recommended that a copy of the completed CMN or DIF be kept in the patient's record. However, neither a physician's order nor a CMN nor a DIF nor a supplier prepared statement nor a physician attestation by itself provides sufficient documentation of medical necessity, even though it is signed by the treating physician or supplier. There must be information in the patient's medical record that supports the medical necessity for the item and substantiates the answers on the CMN (if applicable) or DIF (if applicable) or information on a supplier prepared statement or physician attestation (if applicable).

MPIM ch. 5, § 5.7.

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program unless it is promulgated as a regulation by CMS. However, although not subject to the force and effect of the law, CMS and its contractors, have issued policy and guidelines that describe criteria for coverage for selected types of medical services and supplies.

C. Local Coverage Determinations

The Secretary of HHS requires Medicare contractors to develop and use Local Coverage Determinations ("LCD") to aid in the evaluation of whether a particular service, procedure or item is reasonable and necessary for the treatment of a beneficiary's condition- specifically, when the contractor identifies an item or service that is never covered in certain circumstances and wishes to establish automated review, or when widespread, significant risk to Medicare funds dictates. (CMS, Medicare Program Integrity Manual ("PIM") (Internet-Only Manual Publ'n 100-8) ch.13 § 4.B). The term "LCD" is a creation of the Benefits Improvement and Protection Act of 1997. CMS, PIM ch. 13 §1.3. See also, Act § 1869. Prior to this new terminology, carriers issued Local Medical Review Policies ("LMRP") that served the same purpose and carry the same weight as LCDs. *Id.*

LCDs and LMRPs are used only on a contractor-wide basis and may differ between contractors in different regions of the country. Act § 1869(f)(2)(B). LCDs and LMRPs are binding upon carriers making initial coverage eligibility determinations, but are not binding upon ALJs. Act §1869(f)(2)(A)(i). ALJs and attorney adjudicators and the Council are not bound by LCDs, LMRPs, or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. If an ALJ or attorney adjudicator declines to follow a policy in a particular case, the ALJ or attorney adjudicator decision must explain the reasons why the policy was not followed. An ALJ or attorney

Medicare because its efficacy has not been established. ALJs are not bound by LCDs, LMRPs, or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case.

Considering the evidence in this case, the record demonstrates that Temozolomide in combination with tumor treatment field therapy (HCPCS code E0776) is the best course of treatment for the Appellant to treat his glioblastoma and should be approved by the Plan. The ALJ declines to apply the LCD in this case notwithstanding the fact that the treatment may not be available to other Medicare beneficiaries. The FDA approved the device and found it to be safe and effective in the treatment of glioblastoma. Roger Supp, MD, et. al., *Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma*, Vol. 314 JAMA Number 23 (2015), shows that the device is effective because it significantly prolongs the progression of tumors and increases survival rates. Furthermore, Dr. Abad testified that glioblastoma comes in different types and that the Appellant's type is not amenable to simply being treated with Temozolomide and that the tumor treatment field therapy (HCPCS code E0776) is the Appellant's best hope. The Appellant has exhausted all other treatments and the Appellant has no feasible alternative to treat his glioblastoma. Therefore, based on the professional opinion of the Appellant's neuro-oncologist, the latest peer-reviewed studies of the effectiveness of Temozolomide in combination with tumor treatment field therapy (HCPCS code E0776), and the Appellant's limited options, I conclude the tumor treatment field therapy (HCPCS code E0776) requested by the Appellant is medically reasonable and necessary in this case.

CONCLUSIONS OF LAW


I conclude the Plan is obligated to cover the tumor treatment field therapy (HCPCS code E0776) requested by the Appellant.

ORDER

The Plan is **DIRECTED** to process the claim(s) herein in accordance with this decision.

SO ORDERED

Dated: 7-11-2018


John M. Bergen
U.S. Administrative Law Judge

adjudicator decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect. §405.1062(a)-(b).

Noridian Healthcare Solutions, LLC, developed LCD L34823², *Local Coverage Determination (LCD): Tumor Treatment Field Therapy (TTFT) (L34823)* ("LCD L34823"), effective for services performed after 1/1/17 to aid in the evaluation of when TTFT is covered by Medicare. LCD L34823 states in pertinent part:

In addition to the "reasonable and necessary" criteria contained in this LCD there are other payment rules, which are discussed in the following documents, that must also be met prior to Medicare reimbursement:

- The LCD-related Standard Documentation Requirements Article, located at the bottom of this policy under the Related Local Coverage Documents section.
- The LCD-related Policy Article, located at the bottom of this policy under the Related Local Coverage Documents section.
- Refer to the Supplier Manual for additional information on documentation requirements.
- Refer to the DME MAC web sites for additional bulletin articles and other publications related to this LCD.

For the items addressed in this LCD, the "reasonable and necessary" criteria, based on Social Security Act § 1862(a)(1)(A) provisions, are defined by the following coverage indications, limitations and/or medical necessity.

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

LCD L34823.

Noridian's DME Jurisdiction A manual indicates that Noridian does not cover TTFT.³

ANALYSIS

Notwithstanding the Appellant's arguments to the contrary, the QIC upheld the initial determination and denied coverage of the tumor treatment field therapy (HCPCS code E0776) because the Medicare does not cover such device. For the reasons set forth below, I conclude the tumor treatment field therapy (HCPCS code E0776) requested by the Appellant is covered by Medicare.

LCD L34823, applicable for the State of New York, as well as Noridian's DMEMAC Jurisdiction A supplier manual, both indicate that TTFT is not covered by

² [https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=34823&ver=14&Date=12%2013%2017&DocID=L34823&bc=1AAAAABAAA1AAAAA%3d%3d& \(last visited 5/21/18\)](https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=34823&ver=14&Date=12%2013%2017&DocID=L34823&bc=1AAAAABAAA1AAAAA%3d%3d& (last visited 5/21/18))

³ [https://med.noridianmedicare.com/web/jadme/search-result/-view/2230703/tumor-treatment-field-therapy-tft-response-to-comments \(6/29/18\)](https://med.noridianmedicare.com/web/jadme/search-result/-view/2230703/tumor-treatment-field-therapy-tft-response-to-comments (6/29/18))



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Cleveland, Ohio

Appeal of: [REDACTED]

OMHA Appeal No.: 1-7477540343

Enrollee: [REDACTED]

Medicare: Part C

Medicare No.: *****3949A

Before: John Bergen
Administrative Law Judge

EXHIBIT LIST

EXHIBIT NUMBER	DESCRIPTION	PAGE NUMBERS
1	Organization Determination, MAO Reconsideration and Part C QIC Reconsidered Decision Procedural Documents	1-49
2	Medical Records/Evidence received by MAO and CMS contractors	1-257
3	Request for ALJ Hearing	1-85
4	OMHA Proceedings	1-64
5	Documents Received after Request for ALJ Hearing <ul style="list-style-type: none">Evidence of Coverage	1-290

Dated: 5/1/2018



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Cleveland, Ohio

Appeal of:	OMHA Appeal No.: 1-8045225721
Enrollee	Medicare Part C
Medicare No.:	Before: Brian J. Butler Administrative Law Judge

DECISION

After carefully considering the evidence, arguments and testimony presented in the record, this decision is **FAVORABLE** to the Appellant/Enrollee.

Procedural History

The Appellant requested pre-approval from his Medicare Advantage Plan (MA Plan), Freedom Blue PPO, for coverage of a tumor treatment field therapy (TTFT) device called Optune which was supplied by Novocure, Inc. (Provider). The MA Plan denied the pre-approval request on the basis that a Local Coverage Determination (LCD), L34823, precluded coverage for the device under original Medicare.

The Appellant requested reconsideration. Maximus Federal Services, a Qualified Independent Contractor (QIC), reviewed the case and issued an unfavorable reconsideration decision agreeing that the MA Plan was not required to approve coverage for the device. The QIC cited LCD L34823 in support of the denial.

The Appellant timely filed a request for an Administrative Law Judge (ALJ) hearing. The amount in controversy meets the jurisdictional requirements for a hearing. See 42 C.F.R. §§ 405.1006 and 422.5600(b).

An administrative hearing was held by telephone on November 30, 2018. The Appellant testified at the hearing and was represented by Attorney Bridget Noonan. Dr. Lawrence Kleinberg and Julie Miles, RN, also testified on behalf of the Appellant. In lieu of participating in the hearing, Highmark, the Medicare Advantage Organization that administers Freedom Blue PPO, submitted a position paper which has been incorporated into the record and fully considered in reaching this decision.

All exhibits were admitted into evidence without objection.

Issue

The issue is whether the MA Plan should have granted pre-approval for TTFT to assist with the treatment/management of the Appellant's newly diagnosed glioblastoma.

Findings of Fact

The Appellant, a 69-year old male, presented for a medical evaluation in May 2018 secondary to recurrent mild morning headaches. When working in his yard on June 1, 2018, he developed left-arm numbness that lasted several minutes. The Appellant was concerned about a possible transient ischemic attack and was noted to be hypertensive. He underwent brain imaging which revealed a right-temporal enhancing mass. He then underwent a craniotomy on June 12, 2018 for tumor resection. Pathology was consistent with GBM, IDH-1 wild-type, MGMT not tested. The Appellant was diagnosed with glioblastoma and began radiation with concurrent Temodar which he completed on August 29, 2018. (Exh. 1, p. 28; Exh. 2, pp. 3-44; *Hearing Record*).

On September 5, 2018, the Appellant's physician prescribed TTFT for a period of six months for the treatment/management of malignant neoplasm of overlapping sites of the brain (ICD-10 code C71.8). (Exh. 1, p. 45).

On September 18, 2018, the MA Plan issued a Notice of Denial of Medical Coverage denying coverage for TTFT. The Plan concluded TTFT was considered not reasonable and necessary by Medicare and, therefore, could not be pre-approved. (Exh 1, p. 36).

In April 2011, the Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) approved commercial distribution of the Optune device for treatment of adult patients (22 years of age and older) with histologically-confirmed glioblastoma multiforme (GBM) following histologically- or radiologically- confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. In the pre-market approval letter, CDRH noted the device was intended to be used as a monotherapy, and was intended as an alternative to standard medical therapy for GBM after surgical and radiation options had been exhausted. (Exh. 2, pp. 84-88).

In October 2015, the CDRH issued a pre-market approval supplement for Optune. The supplement approved Optune as a treatment for adult patients (22 years of age or older) with histologically-confirmed GBM and Optune with temozolomide for the treatment of adult patients with newly diagnosed, supranentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant chemotherapy. (Exh. 2, pp. 80-83).

In 2018, the National Comprehensive Cancer Network (NCCN) Guidelines (version 1.2018; March 20, 2018) were updated to include alternating electric field therapy (TTFT) as an NCCN category I recommendation following post-operative standard brain radiation therapy with concurrent temozolomide. (See CD, file "NCCN_CNS_2018.pdf").

By letter dated August 7, 2018, the DME-MAC Medical Directors for Noridian Healthcare Solutions and CGS Administrators confirmed receipt of the Provider's request for formal reconsideration of the TTFT Local Coverage Determination (LCD) coverage criteria. The letter notes that LCD L34823 only addresses coverage criteria of TTFT for recurrent GBM, and not newly diagnosed GBM. The DME-MACs accepted the Provider's request to add coverage guidance for newly diagnosed GBM. A final decision for adding coverage for newly diagnosed GBM was due September 18, 2018. (Exh. 5, pp. 26-28).

By letter dated October 12, 2018, the DME-MAC Medical Directors advised the Provider that the valid request for review of LCD L34823 for coverage of newly diagnosed GBM was subject to the new reconsideration process which went into effect on October 3, 2018. The new process includes utilization of an advisory panel with the publication of a proposed LCD which would then be the subject of a public meeting to consider input from stakeholders and the public with the allowance of an additional 45 days for public comment. The DME-MACs noted they do not have a timeline for the initiation of this new process but assured the Provider they were working diligently on the issue and would provide more definitive details when available. (Exh. 5, pp. 63-64).

Peer-reviewed literature suggests that tumor-treating fields, also known as alternating electric fields, disrupt the cell division process in cancerous tumors which may lead to programmed cell death, or apoptosis. Tumor treating fields have shown statistically significant improvement in patient survival and outcomes in GBM brain tumors compared with traditional standards of care alone. (Exh. 2, pp. 49-79; *See also*, CD, Optune Peer Reviewed Literature; *Hearing Record*).

A large number of health care insurance providers have medical policies in place allowing coverage for Optune for the treatment of glioblastoma multiforme when certain conditions are met. These providers include, but are not limited to AETNA, Highmark, Anthem, Humana, Kaiser, United Healthcare, Cigna, Geisinger, and Blue Cross Blue Shield. (See CD, Optune Medical Policies November 2018; *Hearing Record*).

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an adverse organization determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act (Act) § 1859(g)(5); see 42 C.F.R. § 422.600. The request for hearing is timely filed if filed within 60 days of the date of notice of a reconsidered determination. 42 C.F.R. § 422.602.

In implementing this statutory directive, the Secretary delegated authority to administer the nationwide hearings and appeals system for the Medicare program to the Office of Medicare

Hearings and Appeals (OMHA). See 70 Fed. Reg. 36386, 36387 (June 23, 2005). ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

B. Scope of Review

Medicare Advantage Organization determinations and appeals are governed by the regulations in 42 C.F.R. §§ 422.560 through 422.626. Unless otherwise noted, the ALJ hearing procedures set forth in 42 C.F.R. §§ 405.1000 through 405.1064 apply to Medicare Advantage appeals, to the extent they are appropriate. 42 C.F.R. § 422.562(d).

The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. 42 C.F.R. § 405.1032(a). However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, he or she may notify the parties before the hearing and may consider it an issue at the hearing. *Id.*

C. Standard of Review

The OMHA is staffed with ALJs who conduct de nova hearings. 42 C.F.R. § 405.1000(d). A de novo review means the ALJ reviews the evidence without regard to the findings in the prior determinations on the claim and makes an independent assessment based on the evidence and the controlling laws. However, the burden of proving each element of a Medicare claim lies with the appellant and is satisfied by submitting sufficient evidence in accordance with Medicare rules. See e.g., Act §§ 1814(a)(1), 1815(b), and 1833(e); see also 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, and 405.1030.

II. Principles of Law

A. Statutes and Regulations

Eligibility for Medicare benefits is determined under Title XVIII of the Act, 42 U.S.C. § 1801 et seq., and federal regulations set forth in Title 42 of the Code of Federal Regulations.

The Medicare Part C program establishes standards and sets forth the requirements, limitations, and procedures for Medicare services furnished, or paid for, by Medicare Advantage (MA) organizations through MA plans. See Act § 1851 et seq.; see also 42 C.F.R. § 422.1 (b) et seq. A person is eligible to enroll in Part C if s/he is entitled to Medicare Part A and enrolled in Part B; has not been medically determined to have end-stage renal disease; and meets the applicable residency requirements. See Act § 1851(a)(3)-(b); see also 42 C.F.R. § 422.50(a).

Generally, an MA plan must provide coverage of, by furnishing, arranging for, or making payment for, all services that are covered by Parts A and B of Medicare (Original Medicare) and available to beneficiaries residing in the plan's service area. See Act § 1852(a)(1); see also 42 C.F.R. § 422.101(a). The MAO must disclose the benefits offered under the MA plan, including applicable conditions and limitations, premiums and cost sharing (such as copayments,

deductibles, and coinsurance), and any other conditions associated with receipt or use of benefits. 42 C.F.R. § 422.111.

According to section 1862(a)(1)(A) of the Act, no payment may be made under Original Medicare for any expenses incurred for items or services that are "not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." See 42 U.S.C. § 1395y(a)(1)(A); see also 42 C.F.R. § 411.15(k)(1).

B. Policy and Guidance

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination (NCD), can establish or change a substantive legal standard governing the scope of the benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. NCDs promulgated by the Secretary of HHS under the authority of Section 1862(a)(1) of the Act dictate the criteria under which Medicare covers specified services, procedures or supplies. NCDs are binding upon ALJs. 42 C.F.R. § 405.1060(a)(4); see 42 C.F.R. § 405.1060(b)(1) ("An ALJ may not disregard, set aside or otherwise review an NCD").

Although not subject to the force and effect of law, CMS and its contractors issue policies, manuals and guidelines that describe criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (LCDs). 42 C.F.R. § 405.1062 states that an ALJ is not bound by LCDs or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect.

LCD L34823 entitled "Tumor Treatment Field Therapy (TTFT)" provides that TTFT (E0766) will be denied as not reasonable and necessary.

Medicare Policy Article A52711 provides additional guidance for TTFT, and seems to provide some inconsistent analysis with the LCD, which purports to allow coverage where appropriate and states, as follows:

NON-MEDICAL NECESSITY COVERAGE AND PAYMENT RULES:

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements.

Information provided in this policy article relates to determinations other than those based on Social Security Act §1862(a)(1)(A) provisions (i.e. "reasonable

and necessary"). Tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act §1861(s)(6)). In order for a beneficiary's equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met. In addition, there are specific statutory payment policy requirements, discussed below, that also must be met.

Code E0766 is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling.

Code A4555 is not valid for billing to Medicare. If code A4555 is billed, it will be denied as an invalid code.

CODING GUIDELINES

Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers.

This code is inclusive of all associated supplies necessary for the effective use of code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

Suppliers should contact the Pricing, Data Analysis and Coding (PDAC) Contractor for guidance on the correct coding of these items.

The accompanying Policy Article A52711 establishes that TTFT is categorized under the Durable Medical Equipment benefit. The article explains that code E0766 describes "devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers." The article further states that TTFT devices are in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories.

Analysis

The Appellant seeks pre-approval for TTFT (E0766) to treat newly diagnosed glioblastoma. The MA Plan denied the request because a Medicare local coverage determination states "[t]umor treatment field therapy (E0766) will be denied as not reasonable and necessary." (LCD L34823). For the reasons set forth below, I disagree with the previous denial and conclude that the MA Plan must provide coverage of the requested TTFT for the treatment of the Appellant's newly-diagnosed glioblastoma.

CMS has determined that the TTFT Optune device (E0766) meets the definition of durable medical equipment (DME). (See Policy Article A52711). Medicare covers DME when sufficient information is provided to conclude that the DME was medically reasonable and necessary for the treatment or management of an illness or medical condition. See Act § 1862(a)(1)(A). Generally, CMS and its contractors publish coverage policies and guidance to apply when considering whether or not certain DME is reasonable and necessary. See Act § 1869(f)(2)(B); 42 C.F.R. § 405.1060; *MPIM*, ch 13, § 13.5.1

In this case, there is no Medicare coverage policy currently in place for TTFT for individuals with *newly-diagnosed* GBM. As is noted above, LCD L324823 was previously applied by the MA Plan and the QIC to support the denial. The LCD provides conclusory language stating “[t]umor treatment field therapy (E0766) will be denied as not reasonable and necessary.” The LCD does not elaborate further as to why TTFT is deemed not reasonable and necessary.

Since the publication of this LCD, the DME-MACs, through their medical directors, have conceded that LCD L34823 only precludes coverage of TTFT for *recurrent* GBM as not reasonable and necessary. The DME-MACs have explicitly stated that LCD L324823 does not address coverage for *newly diagnosed* GBM. In the same acknowledgement, the DME-MACs identified new evidence which may support coverage for TTFT treatment for newly diagnosed GBM, including studies published in 2015, 2017, and 2018, and indicated guidance would be forthcoming. (Exh. 5, pp. 26-28). Therefore, it is clear from the record that there is no guidance currently in place for Medicare coverage of TTFT to treat newly diagnosed GBM.

Without applicable coverage guidance from CMS or its Contractors, I must reach an independent determination as to whether TTFT is reasonable and necessary for treatment of the Appellant’s newly diagnosed GBM. To accomplish this, I considered the guidance CMS provides to assist contractors in developing LCDs which is found in Chapter 13 of the *Medicare Program Integrity Manual (MPIM)* and instructs contractors to base LCDs on the strongest evidence available at the time the determination is issued. In order of preference, this evidence includes:

- Published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and
- General acceptance by the medical community (standards of practice), supported by sound medical evidence based on:
 - Scientific data or research studies published in peer-reviewed medical journals;
 - Consensus of expert medical opinion (i.e., recognized authorities in the field); or
 - Medical opinion derived from consultations with medical associations or other health care experts.

MPIM; § 13.7.1.

The manual further explains:

Acceptance by individual health care providers, or even a limited group of health care providers, normally does not indicate general acceptance by the medical community. Testimonials indicating such limited acceptance, and limited case studies distributed by sponsors with financial interest in the outcome, are not sufficient evidence of general acceptance by the medical community. The broad range of available evidence must be considered and its quality shall be evaluated before a conclusion is reached. LCDs which challenge the standard of practice in a community and specify that an item or service is never reasonable and necessary shall be based on sufficient evidence to convincingly refute evidence presented in support of coverage. *MPIM*; § 13.7.1.

In practical terms, this means that to qualify for Medicare coverage, an item or a service (including the DME at issue here) must meet the requirements of a National Coverage Determination (NCD), or a Local Coverage Determination (LCD), or both. If there is no NCD or LCD that is directly on point (as in this case), then there must be published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and general acceptance by the medical community supported by sound medical evidence based on scientific data or research studies in published, peer-reviewed medical journals, consensus of expert medical opinion, or medical opinion derived from consultations with medical associations or other health care experts. (*MPIM*, Chapter 13, §§ 13.5.1, 13.7.1). It is the responsibility of the party seeking Medicare coverage to furnish this information and evidence. See Section 1833(c) of the Act.

In this case, the Appellant has provided evidence which clearly establishes TTFT is safe and effective for its intended use in patients with newly diagnosed GBM. The record contains documentation showing the device received FDA pre-market approval for patients with recurrent GBM in April 2011, and pre-market approval for patients with newly diagnosed glioblastoma in October 2015. While pre-market approval from the FDA does not establish that the device is reasonable and necessary pursuant to Medicare requirements, the approvals do ensure that the FDA determined sufficient scientific evidence exists to show the device was safe and effective for its intended use in patients with newly-diagnosed GBM.

The record further shows TTFT has broad acceptance in the medical community as a safe and effective treatment for GBM. During the hearing, Dr. Kleinberg, a radiation oncologist at Johns Hopkins who is treating the Appellant, testified that the device is not experimental and, in fact, is widely-accepted in the medical community. (*Hearing Record*). I accept Dr. Kleinberg's credible testimony as the doctor is clearly qualified to render this opinion based on his considerable expertise and his experience in treating patients with GBM. Furthermore, Dr. Kleinberg's opinion is fully supported by the clinical research and literature which is contained in the record.

The peer-reviewed literature shows that tumor treating fields disrupt the cell division process in cancerous tumors which may lead to programmed cell death. Tumor treating fields

have also shown statistically significant improvement in patient survival rates and outcomes in GBM brain tumors when compared with the traditional standard of care alone. Additionally, Ms. Miles, a Registered Nurse employed by the Provider who has a great deal of familiarity with Optune, offered credible testimony concerning the effectiveness of the device in treating GBM and its general acceptance in the medical community. In addition to citing the above referenced peer-reviewed literature which supports TTFT to treat newly diagnosed GBM, Ms. Miles noted a number of commercial insurance carriers, including Highmark which is the MA Plan involved in this case, have approved Optune for the treatment of GBM. (*Hearing Record*).

Lastly, in reaching this decision, it is important to note that I considered the arguments in support of the denial from the MA Plan as articulated in the denial letters and the position statement that was submitted prior to the hearing. (Exh. 5, pp. 43-60). The Plan relies heavily on LCD L324823 to support the denial of pre-approval. However, as is set forth above, LCD L324823 has no application here as the DME-MACs have confirmed it applies only to recurrent GBM. The Medical Directors are in the process of developing coverage criteria for TTFT to treat newly diagnosed GBM but, for the time being, no such guidance exists. As such, the MA Plan's reliance on the LCD to deny pre-approval is misplaced.

Furthermore, the MA Plan argues TTFT is experimental in nature. I reject this argument based on the pre-market approval from the FDA, the acceptance of the device from the National Comprehensive Cancer Network, the peer-reviewed medical literature and the credible testimony from Dr. Kleinberg and Ms. Miles establishing that the device is not experimental and has gained wide-spread acceptance in the medical community. I also find it significant that Highmark has approved coverage for TTFT to treat GBM in the commercial setting which undermines any argument from the MA Plan that the device is experimental in nature.

In light of the above, I conclude that TTFT has been proven safe and effective for the treatment of newly diagnosed GBM, and has gained broad acceptance in the medical community. In the absence of coverage guidance from CMS and its contractors that is directly on point for newly diagnosed GBM, I conclude that the record before me clearly establishes that the device is medically reasonable and necessary to treat the Appellant's condition. Therefore, the MA Plan must grant pre-approval for TTFT for the treatment of the Appellant's newly diagnosed GBM.

Order

The MA Plan is **DIRECTED** to process the claim for pre-approval in accordance with this decision.

SO ORDERED.

Dated:

12-10-18



Brian J. Butler

Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Seattle Field Office
Seattle, Washington

Appeal of:	OMHA Appeal No.: 1-7919557871
Beneficiary:	Medicare: Part B
Medicare No.:	Before: Eric K. H. Chinn U.S. Administrative Law Judge

DECISION

After carefully considering the entire record, a **FULLY FAVORABLE** decision is issued for (Appellant).

Procedural History

The Appellant was treated with electronic stimulation cancer treatment, tumor treatment field therapy (CPT code E0766) (TTFT) (also known as Optune) on November 19, 2017, December 19, 2017 and January 19, 2018 (Exh. 1, pp. 19–21; Exh. 2). A claim for the TTFT was submitted to Part B Durable Medical Equipment Medicare Administrative Contractor, CGS (DME MAC), which was denied initially and upon redetermination (Exh. 1, p. 11). On August 31, 2018, Qualified Independent Contractor, C2C Solutions, Inc. (QIC) issued an unfavorable reconsideration decision and held the supplier liable for the non-covered charges (Exh. 1, pp. 1–6). The Appellant submitted a timely request for an Administrative Law Judge (ALJ) hearing to the Office of Medicare Hearings and Appeals (OMHA) on October 1, 2018 (Exh. 3, pp. 1–4). The amount in controversy meets the jurisdictional requirement for a hearing before OMHA (*Id.* at 19–21).

Pursuant to proper notice, Appellant's hearing was conducted by telephone on November 7, 2018 (Exh. 4; Hearing CD). Appellant appeared through his Attorney Debra Parrish and witness, Julie Miles, RN (Clinical Appeals Specialist), who testified (Hearing CD). No other person appeared for the hearing (*Id.*). Under rules governing ALJ review, evidence not submitted by the Medicare provider or supplier before the issuance of the QIC's reconsideration decision must be accompanied by an explanation addressing why such evidence was not previously submitted to the QIC or a prior decision maker. 42 C.F.R. § 405.1018. Along with his request for an ALJ hearing, the Appellant submitted additional documents that were either duplicative or requested by the ALJ during the hearing (*Id.*). Good cause was established for admitting all of the documentation (*Id.*). Exhibits 1–6 were admitted without objections (*Id.*).

Issues

Whether the TTFT provided to the Appellant on the dates of service were reasonable and necessary for purposes of coverage under Medicare Part B; and if not, whether and to what extent Appellant (or any other party) may be liable under section 1879 of the Social Security Act (Act).

Findings of Fact

Based on the record as a whole, a preponderance of the evidence established the following:

1. The 76 year-old male Appellant was newly diagnosed with glioblastoma multiforme (GBM) in April 2017 (Exhibit 2; Testimony). A magnetic resonance image (MRI) of the Appellant's brain showed a 7-mm left temporal lobe lesion with surrounding vasogenic edema (Exh. 2, pp. 27-34; Testimony). The Appellant underwent a maximal safe resection and pathology confirmed a left temporal astrocytoma WHO grade II (*Id.*).
2. The plan of care included hypofractionated radiation therapy (course of 40.05 Gy in 15 fractions), which was completed on May 22, 2017 (*Id.* at 33). Status post-maximal safe resection, there were no residual tumors seen on the Appellant's follow-up MRI (Exh. 2, p. 26; Testimony).
3. M.D., signed prescriptions for Optune to treat the Appellant's left temporal anaplastic astrocytoma WHO grade II (Exh. 2, pp. 1-2). Optune is approved by the Food and Drug Administration (FDA) for treating recurrent and newly diagnosed GBM tumors (Exh. 1, pp. 25-74; Testimony).
4. The Appellant was treated with TTFT on November 19, 2017, December 19, 2017 and January 19, 2018 (Exh. 1, pp. 19-21; Exh. 2). TTFT inhibits cancer cell replication by interfering with the proper formation of the mitotic spindle during anaphase and by causing intracellular dislocation of macromolecule and organelles (Exh. 1, pp. 31-34).
5. Peer-reviewed literature shows the improved clinical outcome of patients who receive TTFT for their GBM (Exh. 1; Testimony). TTFT for GBM is included in the National Comprehensive Cancer Network (NCCN) guidelines (*Id.*).
6. The DME MAC Directors (DMD) informed the supplier in this case that it was conducting a formal reconsideration of LCD L34823, which would include collecting and considering input from experts in the area of clinical oncology and related fields (Exh. 6, p. 2; Testimony).

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act (Act) § 1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. The ALJs within OMI-IA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council.

A hearing before an ALJ is only available if the remaining amount in controversy is \$160.82 Fed. Reg. 45592 (Sept. 29, 2017) (setting the 2018 amount in controversy threshold amount at \$160). The request for hearing is timely if filed within sixty days after receipt of the QIC's reconsideration decision. 42 C.F.R. § 405.1002.

B. Scope of Review/ Standard of Review

The ALJ conducts a *de novo* review and issues a decision based on the hearing record. 42 C.F.R. § 405.1000(d). *De novo* review means the ALJ reviews the evidence without regard to prior findings made on the claim, and makes an independent assessment based on the evidence and controlling laws and policy. The burden of proving each element of a Medicare claim lies with the appellant, and is satisfied by submitting sufficient evidence in accordance with Medicare requirements. Act §§ 1814(a)(1), 1815(b), and 1833(e); 42 C.F.R. §§ 405.1018, 405.1028, 405.1030 and 42 C.F.R. § 424.5(a)(6).

II. Principles of Law

A. Social Security Act and Code of Federal Regulations

The Medicare program is administered through the Centers for Medicare and Medicaid Services, a component of the United States Department of Health and Human Services (HHS). The Secretary or HHS is authorized to enter into contracts with private entities for the day-to-day operations of the program, for claims for durable medical equipment, prosthetics, orthotics, and supplies. DME MACs administer the processing of the claims. Act § 1842(a) (1) (A).

Part B of the Act provides coverage for a variety of medical services and supplies furnished by physicians, or by others in connection with physicians services, for outpatient hospital services, and for a number of other specific health-related items and services. Section 1862(a)(1) of the Act excludes Medicare payment for services which "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Carriers shall, at the request of a supplier or beneficiary, determine in advance of delivery of an item whether payment for the item may not be made because the item is not covered if the item is a customized item the patient to whom the item is to be furnished, or the supplier, requests that such advance determination be made, and the item is not an inexpensive item as specified by the Secretary. Act § 1834 (a) (15) (C). The benefits provided to an individual by the

insurance program established by this part shall consist of, in part, as (l) entitlement to have payment made to him or on his behalf (subject to the provisions of this part) for medical or other health services . . . Act § 1832(a). The term "medical and other health services" includes durable medical equipment. 42 CFR § 414.902 defines durable medical equipment as equipment furnished by a supplier or a home health agency that

- (1) can withstand repeated use;
- (2) is primarily and customarily used to serve a medical purpose;
- (3) generally is not useful to an individual in the absence of an illness or injury; and
- (4) is appropriate for use in the home.

42 CFR § 410.38(a) provides, in pertinent part, as follows regarding the scope and conditions of durable medical equipment:

Medicare Part B pays for the rental or purchase of durable medical equipment including iron lungs, oxygen tents, hospital beds, and wheelchairs, if the equipment is used in the patient's home or in an institution that is used as a home.

B. CMS Manual System and Local Policy

The manuals issued by the Centers for Medicare and Medicaid Services (CMS) administering the Medicare program are also considered. Although not binding on the ALJ, the respective manuals provide guidance in the administration of the Medicare program. In *Shalala v. Guernsey Memorial Hospital*, 514 U.S. 87, 102 (1995), the United States Supreme Court concluded that an agency manual section is a valid interpretive rule and that it is reasonable for the agency to follow it. CMS, Medicare Benefit Policy Manual (MBPM) (Internet-Only Manual Publ'n 100-2) ch. 15, § 110, provides general coverage guidelines for durable medical equipment.

CGS Administrators, Local Coverage Determination L34823: Tumor Treatment Field Therapy (LCD L34823) (effective Jan. 2017), which provides, in relevant part, that tumor treatment field therapy (E0766) will be denied as not reasonable and necessary (Exh. 6, pp. 17–19).

Analysis

The QIC denied payment because it concluded the published studies in the medical literature did not clearly document the effectiveness of the TTFT. The QIC also relied on LCD L34823 to deny coverage for the TTFT. However, after reviewing the entire record, it was determined that the TTFT provided to the Appellant is covered under Part B of Medicare. Medicare is a defined benefit program, which means that it does not cover all available medical services and supplies. Medicare does not cover medical services that are not medically reasonable and necessary. LCD L34823 provides that TTFT will be denied as not reasonable and necessary, and pursuant to 42 C.F.R. § 405.1062(a), an ALJ must give substantial deference to local coverage determinations. If an ALJ declines to follow a local coverage determination, the ALJ

must explain the reason why the policy was not followed in accordance with 42 C.F.R. § 405.10620(b).

LCD L34823 should not be followed in this case because it does not identify any justification for the denial of all TTFT as not reasonable and necessary. Additionally, the record includes documentation from the DMD that LCD L23823 is currently being reconsidered and possibly written to establish new coverage guidelines for TTFT after considering input from experts in the area of clinical oncology and other related fields. Furthermore, the record supports that TTFT is an effective treatment of newly diagnosed cases of GBM, and it is FDA approved for it. Lastly, the record contains peer-reviewed literature that shows improved clinical outcome of patients who received TTFT for their GBM.

In conclusion, the record supports that TTFT was properly prescribed for the Appellant and is medically reasonable and necessary to treat him as he was newly diagnosed with GBM. Based on the above, the TTFT provided to the Appellant on each of the dates of service was medically reasonable and necessary.

Conclusions of Law

The TTFT provided to the Appellant on each of the above-referenced dates of service was medically reasonable and necessary. Accordingly, the TTFT (E0766) provided to the Appellant on said dates of service is reimbursable under Part B of Medicare.


Order

The Medicare contractor is **DIRECTED** to process Appellant's claim consistent with this decision.

SO ORDERED

Dated:

NOV 20 2018



Eric K. H. Chinn
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Irvine Field Office
Irvine, CA

Appeal of:	ALJ Appeal No.: 1-5320044848
Beneficiary:	Medicare: Part C
HICN: *** **	Before: Michael Ciani U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented, a **FULLY FAVORABLE** decision is entered for (Appellant).

Procedural History

Appellant requested Blue Shield Blue Cross of Michigan (BSBC) to pre-approve coverage for an electrical stimulation device used for cancer treatment (HPCS E0766). The tumor treatment field therapy (TTFT) called Optune, is supplied by Novocure, Inc. (Provider). BSBC denied the pre-approval initially and on appeal, on the basis that a Local Coverage Determination (LCD) (L34823) precludes payment. The LCD states TTFT treatments are not medically reasonable and necessary. Independent Review Entity MAXIMUS Federal Services (the IRE) also denied pre-approval of the Optune on the same basis. Appellant timely filed a request for a hearing before an Administrative Law Judge (ALJ) and the amount in controversy meets the jurisdictional requirement for this action. See 42 C.F.R. §§ 405.1006 and 422.600(b).

The evidence in the record indicates that Optune is a portable, wearable medical device that delivers TTFT to a targeted tumor. On April 8, 2011, the FDA approved TTFT for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy and as an alternative to standard medical therapy for glioblastoma multiforme after surgical and radiation options have been exhausted.

In 2015, Optune received additional pre-market approval from the FDA for newly diagnosed glioblastoma in combination with temozolomide after standard surgical resection and radiation therapy. The Provider is the sole global supplier for the Optune System and they are currently out-of-network with BSBC.

Pursuant to proper notice, Appellant's telephonic hearing was conducted on November 30, 2016. Appointed Representative from Novocure Team Leader Ms. Tanya Lane appeared for Appellant and provided testimony. Ms. [redacted] Appellant's daughter also provided testimony on behalf of Appellant. Dr. [redacted], prescribing and treating physician, provided expert testimony on behalf of Appellant. BSBC timely elected to appear as a party and testified through its representative Ms. Carmen Andersen. Exhibits were admitted into the record without objection. Additionally, the undersigned took administrative notice of two medical literature documents pertaining to TTFT, one by Group Health, referred to as a Clinical Review Criteria, the other by Health Net, Policy number NMP523 updated May 2016. Both summarize recent Optune uses and clinical studies and note improved survival rates using the Optune treatment. Excerpts were attached to the record. Furthermore, the undersigned took administrative notice of the applicable LCD, L34823 and citations to authority, and MAC decision M-15-1354, which involved TTFT, and a recent Novocure press release which announced that as of May 4, 2016, BCBS of Michigan would offer Optune coverage as a treatment, excerpts also attached. Appellant's representative and BSBC knowingly and voluntarily waived right to counsel.

Issues

Whether BSBC is required to cover the TTFT (Optune) and whether an out-of-network exception should be granted?

Relevant Facts in the Record

The record indicates Appellant requested BSBC to pre-approve coverage for Optune Plus Transducers for recurrent glioblastoma. Appellant was diagnosed with recurrent glioblastoma in May of 2015. Appellant received concurrent Temodar and radiation and completed treatment on July 27, 2015. Appellant began Temozolomide cycles of 5 days every 28 days. Chemo-radiation was completed by August 2015. On June 22, 2016, magnetic resonance imaging showed post-treatment changes. Appellant subsequently underwent resection of the tumor on July 8, 2016.

After discussing treatment options, with Appellant, Appellant's treating physician, Dr. [redacted] decided that Optune would be the best therapy for Appellant. Given the aggressive nature and extremely limited treatment options of Appellant's disease, Dr. [redacted] strongly recommends Appellant receive coverage for Optune, as he contends that it is the best FDA approved option at this time for treating recurrent glioblastoma. (Exh. 1 at 15-17; Exh. 4 at 34; Hearing Record).

Dr. [redacted] testified further that this treatment is the best hope for slowing down the progression of Appellant's disease, which has come back. (Exh. 1 at 15-17; Hearing Record). Dr. [redacted] testified he has used Optune for patients, as well as observing the results of other patients through multiple clinical trials, and opines that the Optune treatment is medically reasonable and necessary for Appellant. Moreover, in his medical opinion, the Optune treatment statistically speaking provides patients with a forty per cent survival rate over two years, a substantially greater percentage increase for survival than without use of Optune. (Hearing Record). He has also stated that he is aware of multiple medical insurance payer entities that

cover Optune, which in his view necessarily means the treatment is viewed in the medical community as being medically reasonable and necessary. Additionally, he noted peer consensus at a recent formal meeting of the Society of Neurology & Oncology, opining that the Optune treatment has been the break-through treatment in the last ten years for this type of brain cancer and that his peers likewise agree and use Optune. (Hearing Record).

Ms. Lane of Novocure testified for Appellant requesting the undersigned approve coverage for Appellant. She stated that approximately one hundred medical insurance payer entities now approve coverage for Optune and therefore find the treatment to be medically reasonable and necessary. Moreover, she testified BSBC of Michigan, the payer here, now approves coverage of Optune for "commercial" non-Medicare plans, inferring that it already finds Optune to be medically reasonable and necessary, and therefore all patients covered by BSBC's other plans have coverage for Optune. She further testified Optune has been approved by several ALJ decisions. Moreover, she indicated the revised LCD applicable here, which has been used as the mechanism to deny Optune to Appellant, contains only those outdated citations to authorities which have not been updated and do not incorporate the recent successful clinical trials and studies Optune has had over the last year. Furthermore, Optune is FDA approved. (Hearing Record; See Exh.1 at 326-341 for some noted clinical trial summaries and results). One in particular involved over three hundred patients and concluded an increased survival rate over several months.

There is no issue that Appellant is medically cleared and qualifies for the Optune treatment.

Ms. Anderson testified for the Plan and indicated the Plan's position was still essentially the same, that is, since Original Medicare would not provide coverage on the basis of the LCD, it would not. She had no knowledge of any medical evidence in the record which would not otherwise support a conclusion that Optune was not medically reasonable and necessary in this case. Moreover, she had no specific knowledge that BSBC of Michigan has recently allowed coverage for Optune. In other words, the Plan has not rebutted any of the medical evidence in the record that establishes the Optune treatment is medically reasonable and necessary for Appellant.

A copy of Appellant's Plan Evidence of Coverage appears in the record at Exh. 1 at 1-254. The Plan is described as Medicare Plus Blue and is a PPO plan. The undersigned finds some significance to the language in the Plan which states in the coverage chart at Exh. 1 at 140 for 2016 coverage options and which provides a specific exception to allow coverage (for otherwise non-covered treatments even if Medicare does not cover the treatments). The language in the Plan states: "Services considered not reasonable and necessary according to the standards of Original Medicare (are not covered) unless these services are listed by our plan as covered services." As testified to by Ms. Lane and as shown in the press release, as of May 4, 2016, BSBC of Michigan plans allow for coverage of the Optune treatment. While Ms. Anderson could not address these recent changes, nor provide any opinion regarding how this change may impact Appellant's case, it is clear to the undersigned that BSBC of Michigan now views the Optune treatment as being medically reasonable and necessary, and by the contractual language in its own Plan, BSBC is not bound to follow the LCD.

Appellant therefore requests approval of the Optune treatment and approval for an out-of-network exception so that Appellant can access Optune under its network benefits.

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an adverse organization determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act (Act) § 1859(g)(5); *see* 42 C.F.R. § 422.600. The request for hearing is timely filed if filed within 60 days of the date of notice of a reconsidered determination. 42 C.F.R. § 422.602.

In implementing this statutory directive, the Secretary delegated authority to administer the nationwide hearings and appeals system for the Medicare program to the Office of Medicare Hearings and Appeals (OMHA). *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

B. Scope of Review

Medicare Advantage Organization determinations and appeals are governed by the regulations in 42 C.F.R. §§ 422.560 through 422.626. Unless otherwise noted, the ALJ hearing procedures set forth in 42 C.F.R. §§ 405.1000 through 405.1064 apply to Medicare Advantage appeals, to the extent they are appropriate. 42 C.F.R. § 422.562(d).

The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. 42 C.F.R. § 405.1032(a). However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, he or she may notify the parties before the hearing and may consider it an issue at the hearing. *Id.*

C. Standard of Review

OMHA is staffed with ALJs who conduct *de novo* hearings. 42 C.F.R. § 405.1000(d). A *de novo* review means the ALJ reviews the evidence without regard to the findings in the prior determinations on the claim and makes an independent assessment based on the evidence and the controlling laws. However, the burden of proving each element of a Medicare claim lies with the appellant and is satisfied by submitting sufficient evidence in accordance with Medicare rules. *See e.g.*, Act §§ 1814(a)(1), 1815(b), and 1833(e); *see also* 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, and 405.1030.

II. Principles of Law

A. Statutes and Regulations

Eligibility for Medicare benefits is determined under Title XVIII of the Act, 42 U.S.C. § 1801 et seq., and federal regulations set forth in Title 42 of the Code of Federal Regulations.

The Medicare Part C program establishes standards and sets forth the requirements, limitations, and procedures for Medicare services furnished, or paid for, by Medicare Advantage (MA) organizations through MA plans. *See* Act § 1851 et seq.; *see also* 42 C.F.R. § 422.1(b) et seq. A person is eligible to enroll in Part C if s/he is entitled to Medicare Part A and enrolled in Part B; has not been medically determined to have end-stage renal disease; and meets the applicable residency requirements. *See* Act § 1851(a)(3) – (b); *see also* 42 C.F.R. § 422.50(a).

Generally, an MA plan must provide coverage of, by furnishing, arranging for, or making payment for, all services that are covered by Parts A and B of Medicare (Original Medicare) and available to beneficiaries residing in the plan's service area. *See* Act § 1852(a)(1); *see also* 42 C.F.R. § 422.101(a). The MAO must disclose the benefits offered under the MA plan, including applicable conditions and limitations, premiums and cost sharing (such as copayments, deductibles, and coinsurance), and any other conditions associated with receipt or use of benefits. 42 C.F.R. § 422.111.

According to section 1862(a)(1)(A) of the Act, no payment may be made under Original Medicare for any expenses incurred for items or services that are “not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *See* 42 U.S.C. § 1395y(a)(1)(A); *see also* 42 C.F.R. § 411.15(k)(1).

B. Policy and Guidance

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination (NCD), can establish or change a substantive legal standard governing the scope of the benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. NCDs promulgated by the Secretary of HHS under the authority of Section 1862(a)(1) of the Act dictate the criteria under which Medicare covers specified services, procedures or supplies. NCDs are binding upon ALJs. 42 C.F.R. § 405.1060(a)(4); *see* 42 C.F.R. § 405.1060(b)(1) (“An ALJ may not disregard, set aside or otherwise review an NCD”).

Although not subject to the force and effect of law, CMS and its contractors issue policies, manuals and guidelines that describe criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (LCDs). 42 C.F.R. § 405.1062 states that an ALJ is not bound by LCDs or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect. (emphasis added).

LCD L34823 entitled “Tumor Treatment Field Therapy (TTFT)” provides that TTFT (E0766) will be denied as not reasonable and necessary.

The undersigned notes that the LCD contains a blanket citation to authorities for support but provides no rationale, discussion or criteria upon which exceptions can be made within the

context of the LCD, or upon which the LCD is based. Moreover, it does not discuss what authorities it specifically relies upon, nor what the authorities purport to state.

Policy Article A52711 provides additional guidance for TTFT, and seems to provide some inconsistent analysis with the LCD, as follows:

NON-MEDICAL NECESSITY COVERAGE AND PAYMENT RULES:

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements.

Information provided in this policy article relates to determinations other than those based on Social Security Act §1862(a)(1)(A) provisions (i.e. "reasonable and necessary"). **Tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act §1861(s)(6)).** In order for a beneficiary's equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met. In addition, there are specific statutory payment policy requirements, discussed below, that also must be met.

Code E0766 is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling.

Code A4555 is not valid for billing to Medicare. If code A4555 is billed, it will be denied as an invalid code.

CODING GUIDELINES

Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers.

This code is inclusive of all associated supplies necessary for the effective use of code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

Suppliers should contact the Pricing, Data Analysis and Coding (PDAC) Contractor for guidance on the correct coding of these items.

The accompanying Policy Article A52711 therefore establishes that TTFT is categorized under the Durable Medical Equipment benefit. The article explains that code E0766 describes "devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers." The article further states that TTFT devices are in the frequent and substantial service payment

category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. While it defers to any applicable LCD it seems to confirm categorically that in particular cases such treatments should be found to be medically reasonable and necessary. Additionally, it anticipates that any applicable LCD will provide eligibility criteria.

Analysis

After careful consideration of the evidence and arguments presented, the undersigned finds that the Optune treatment is reasonable and necessary for purposes of coverage under Medicare, and that out-of-network coverage is warranted.

The policy letter and the underlying analysis that went into it clearly anticipate that there are situations where the Optune treatment would be medically reasonable and necessary, and it can be approved as Part B DME. It ultimately defers to any LCD which may be applicable. Clearly the policy letter provides policy support that the treatment has merit and could qualify as a covered DME under the Act. The undersigned finds this to be significant in this case, but certainly not dispositive. The undersigned finds the extensive medical evidence in the record to be dispositive. The medical evidence establishes the Optune treatment is medically reasonable and necessary for Appellant. Appellant has carried his burden of proof. This evidence includes the letter and testimony of the treating doctor, Ms. Lane's testimony, the reversal by BSBC of Michigan's position allowing coverage of Optune under its plans, the Plan's language, and the numerous medical literature articles, and recent studies, submitted by Novocure contained in Exh.1 and Exh. 4.

The undersigned finds the Plan's change of opinion regarding coverage for Optune (since May 2016) significant. The language in Appellant's Part C Plan clearly states coverage for Optune is mandated here, regardless of whether Original Medicare covers it, since now BSBC offers coverage. To grant coverage to 4.6 million people in Michigan but deny Appellant coverage because he is on a Medicare Plan is ludicrous, arbitrary and capricious. In any event, regardless of the Plan's own language and coverage determinations, the undersigned declines to give substantial deference to the LCD in this case. Original Medicare should cover the treatment because the LCD is not applicable in this particular case. The extensive medical record establishes the treatment is medically reasonable and necessary for Appellant.

To be clear, this appeal addresses whether BSBC is required to cover the Optune treatment at issue, to this particular Appellant. The IRE concluded that BSBC did not have to provide pre-approval for the device based on LCD L34823 that states that TTFT will be denied as not reasonable and necessary. The LCD is void of any rationale or discussion and merely cites certain authorities, which according to Ms. Lane and on their face, are outdated, and cannot be relied upon in this case. While giving due consideration to the LCD the undersigned finds the LCD cannot be followed in this case for a multitude of reasons

First, the medical evidence is overwhelming and unrebutted by the Plan, that Optune is medically reasonable and necessary for Appellant. It is clear that Appellant suffers from glioblastoma multiforme, an aggressive form of brain cancer. He has had extensive treatment including surgery and radiation. He, now on the advice of his medical treating doctor, seeks coverage of the Optune treatment services furnished by Novocure. (Exh. 1 at 15-17). The Optune treatment is highly recommended by his doctor, who has used the treatment successfully. Optune uses

alternating electrical fields to interfere with the division of malignant cells. The electric fields treatment disrupts the rapid cell division exhibited by cancer cells. A recent medical study of a large clinical trial shows that Optune treatment had minimal risks, and combining it with the drug Temozolomide, may show even more significant overall survival by several months. (Exh. 1 at 13, 15-17; Exh. 1 at 337-338). According to Appellant's treating doctor, with Optune patients have a forty per cent chance of surviving two years. As Dr. [redacted] testified to, this amounts to the best break-through results for treatment of this disease in a decade. (Hearing Record).

In weighing the evidence, the undersigned has extensive medical evidence in the record establishing the Optune treatment in all medical probability would greatly enhance the life span of Appellant, and while the treatment is expensive, it would be comparable to using other chemotherapy drugs if those options were available to Appellant. ([redacted] Lane, Hearing Record).

Second, on the other side, the Plan has provided no medical evidence to cast any doubt about the effectiveness of the treatment, especially as applied to treating Appellant. Indeed, it has done just the opposite but approving the treatment for all of its other plans. (Lane, Hearing Record). The Plan cannot assert the treatment is medically reasonable and necessary for all other patients in Michigan but argue it is not for Medicare Part C Plan patients. Its own contractual language dictates the Optune treatment should be provided to Appellant.

Third, the basis for the denial was based upon erroneous assumptions, and the LCD does not contain any discussion, rationale, or list any criteria for exceptions or eligibility. Further, the Plan does not contain any explanation for how it reached its denial conclusion, nor does the LCD explain its conclusion. In a case narrative summary attempting to justify the denial decision by the Plan and presumably citing the Plan's rationale, the IRE justification recital follows an erroneous Catch 22 logic, stating the Optune will be denied because the LCD says it will be denied because it is not reasonable and necessary because that is what was said in the LCD. It also erroneously states that the treatment equates to being experimental in nature and as such would only be covered if approved by Original Medicare or under an approved clinical research study or by its plan. (Exh. 1 at 4-5). Of course, BSBC does not view it as experimental now since it covers the Optune treatment in all of its other plans, and has done so since May 2016. Moreover, it has been FDA approved for use twice, in 2011 and in 2015, hence it is not deemed experimental for Appellant's anticipated use.

Fourth, Appellant's treating physician, Dr. [redacted] prescribed Optune due to the aggressive nature and extremely limited treatment options of Appellant's disease. In support of his position, and highly probative, Dr. [redacted] confirms that the National Comprehensive Cancer Network (NCCN) Guidelines were recently updated to include the Optune treatment for recurrent glioblastoma. Exh. 1 at 15; See also at 290).

Here, the medical evidence clearly establishes that the Optune treatment is medically reasonable and necessary based on Appellant's diagnosis and on the fact that Appellant has tried and exhausted all chemotherapy and radiation therapy, in addition to surgical treatment. BSBC and the IRE denied pre-approval for the TTFT solely based on the conclusion reached in the LCD.

Additionally, the testimony of Ms. Lane that the LCD is outdated is very probative and the undersigned gives it great weight and as applied to this case. In her view, the LCD ignores

medically relevant criteria, medical opinions, and recent studies and clinical trials, which support a finding that the Optune treatment is medically reasonable and necessary for Appellant.

Federal regulations permit an ALJ to decline to follow a local coverage policy in an individual case. 42 C.F.R. Sec. 405.1062. The undersigned therefore has considered, yet declines to defer to LCD L34823 in this case.

The medical evidence in this administrative record establishes the treatment is medically reasonable and necessary. In fact, there is no evidence to the contrary in the record. The LCD categorically denies that the treatment is reasonable and necessary under any circumstance without setting forth any underlying basis or discussion or criteria, for that determination.

The undersigned recognizes there is a contrary MAC decision which reversed one ALJ decision pertaining to TTFT, although this may be an anomaly since Ms. Lane indicates several ALJ decisions have been in favor for Optune treatment and have apparently not been reversed. In any event, the undersigned finds that case is distinguishable, and the holding in that decision is now outdated.

That case, M-15-1534, focused on what it perceived as the ALJ decision striking down the entire LCD. The result in that MAC decision also relied heavily upon the citation to authorities in the LCD, presumably to reach its conclusion that there was some doubt at the time the LCD was enacted, about the effectiveness of the Optune treatment within the medical community. Based upon that record, the MAC found an insufficient record was established to support the ALJ's decision not to defer to the LCD. Certainly, this case and the undersigned's decision herein do not involve a challenge to the LCD (pursuant to Part 426 or otherwise), and the legal stature of the LCD is not an issue here.¹

¹ The MAC decision also criticizes the deciding ALJ decision it reversed indicating the decision did not explain the significance of the various medical literature which was admitted into evidence to support the premise that the Optune treatment is effective. The MAC decision infers the medical evidence in that case relied solely upon this medical literature. That is not the situation here. The testimony of the treating doctor, and Ms. Lane, in addition to the medical literature and new studies and clinical trials, as well as evidence that a significant number of medical insurance payers now provide coverage for Optune, establish the medical community accepts Optune as a break-through brain cancer treatment. Moreover, the MAC decision indicates in its last paragraph that the LCD will eventually be updated if warranted and if the medical literature substantially establishes the validity of the treatment. However, circumstances have changed since issuance of that decision. The MAC decision was decided almost a year ago and the underlying evidentiary record in the ALJ decision goes back even further. The LCD has not been substantially revised towards coverage nor has it addressed the significant medical advances of the Optune treatment, as testified to by Appellant's treating doctor and Ms. Lane. Additionally, Ms. Lane's testimony establishes that the sources cited in the LCD are outdated and not valid, and that a July revision was in essence pro forma. Indeed, it appears as though not all of the old sources cited in the LCD even reach the consensus conclusion in the LCD as two of the cited sources cite to the Novocure website and Novocure's safety summary, and a third cites to a Novocure sponsored study, cite source 7, as reflected and commented upon in cite source 11. This source 11 was published by the Australian Government and published in 2009, which pre-dates even FDA approval of Optune. It in fact notes some survival rates based upon two small studies and recommends monitoring the effectiveness of Optune over a 24 month period. In any

That being said, clearly it is appropriate for the undersigned to analyze any perceived deficiencies in the LCD and its rationale, the current state of the medical community's view of the Optune treatment, and the current validity of the underlying sources cited in the LCD, otherwise the undersigned would never know when to defer or not defer. In this regard, it is noteworthy that the MAC decision is already almost one year old. During 2016, the medical community has more favorably embraced the Optune treatment. Moreover, the evidence in the record establishes the authorities the LCD relied upon, are now outdated and do not necessarily reflect the consensus of the medical community.

In this context, the sparse nature of any medical reasoning in the LCD provides additional reasons not to follow it here, where the medical evidence in this record, is so overwhelming that in this Appellant's case, the Optune treatment is more likely than not, going to increase his life span survival by several months, or more. It is also significant that since the MAC case was decided additional studies have proven the effectiveness of the Optune treatment during this period, and as noted earlier, by the change of position in many medical insurance entities, including BSBC of Michigan, the sponsor of the Plan here. Indeed, BSBC of Michigan itself now provides Optune coverage. In the Novocure press release referenced above, dated May 4, 2016, which the undersigned took administrative notice of, it was declared that now "[m]ore than 112 million Americans now have coverage of Optune as a treatment for newly diagnosed and/or recurrent glioblastoma" adding 4.6 million covered individuals with the addition of BSBC Michigan. (Record excerpt). This adds to positive coverage from Regence BSBC, Preferred One, Univera Healthcare, Asuris Northwest Health, and Group Health Cooperative Washington and Idaho, all implemented since March 2016. (*Id.*)

Moreover, the undersigned finds Ms. Lane's testimony probative that the authorities cited by the LCD are now largely outdated and the latest revisions to the LCD do not consider the new clinical trials and studies described by Ms. Lane and Dr. Chinnaiyan, and the accompanying medical literature in the record. For instance, citing from a BSBC article contained in the case file, *BCN Provider News*: "The safety and effectiveness of TTF therapy is established for the treatment of supratentorial glioblastoma. TTF therapy may be medically necessary when used under the care of a physician, in adults 22 years and older and as an adjunct therapy to standard therapy." (Exh. 4 at 102; See also conclusions from *Journal of the American Medical Association* at Exh. 4 at 107).

Under the regulations, which unlike policy, has the force and effect of law, the undersigned ALJ has the authority to carefully consider the LCD and then elect to depart from it based upon the evidentiary record. Here, the medical evidence in the administrative record supports the finding that for Appellant the Optune treatment is medically reasonable and necessary.

event, on their face, the citation dates for each source cited in the LCD corroborates Ms. Lane's testimony that they have not been updated. Appellant has no time to await future administrative revisions. It is clear that the LCD has not kept pace with the medical technology and literature, and the LCD cannot be relied upon in this particular case to deny the treatment to Appellant, where all of the admitted medical evidence in this record supports a finding that the treatment is medically reasonable and necessary for this Appellant at this time. It is clear that the treatment has worked for many patients and has been approved by various medical institutions in particular cases, and will in all medical probability be successful for Appellant. (Exh. 1 at 15-17).

In addition to research articles submitted in support of the conclusion that Optune is safe and effective in treating Appellant's condition, including the aforementioned *BCN News* excerpt, the undersigned finds the testimony of the treating doctor, Dr. (Exh. 1 at 15-17) to be highly probative. The Optune treatment has dramatically expanded survival rates for the type of aggressive brain cancer from which Appellant suffers from. The LCD does not consider or address these recent break-through results or general acceptance consensus from the medical community and accordingly the undersigned will not defer to it in this particular case.

The undersigned therefore finds that the TTFT device known as Optune, is medically reasonable and necessary for Appellant. In addition, the Provider is entitled to an in-network exception because there are no in-network providers of the device. BSBC must provide supplemental coverage for the TTFT at issue. The medical record contains sufficient documentation of Appellant's disease to substantiate the medical reasonableness and necessity for the Optune treatment at issue, satisfying Medicare rules and regulations.

Conclusions of Law and Order

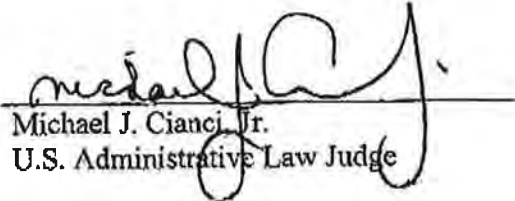
For the reasons above, BSBC of Michigan and/or its affiliates, is required to provide coverage for the Optune treatment.

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: _____

DEC 12 2016


Michael J. Cianci, Jr.
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Irvine Field Office
Irvine, CA

Appeal of:

ALJ Appeal No.: **1-7141790809**

Beneficiary:

Medicare: **Part C [EXPEDITED]**

HICN:

***.**1953D6

Before:

Michael Cianci

U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented, a **FULLY FAVORABLE** decision is entered for (Appellant).

Procedural History

Appellant requested pre-approval coverage from her Plan, Humana Health Plan, Inc., for an electrical stimulation device used for cancer treatment (HCPCS E0766). The tumor treatment field therapy (TTFT) called Optune, is supplied by Novocure, Inc. (Provider). The Plan denied the pre-approval initially and on appeal, on the basis that a Local Coverage Determination (LCD) (L34823) precludes payment. The LCD states TTFT treatments are not medically reasonable and necessary. Independent Review Entity MAXIMUS Federal Services (the IRE) also denied pre-approval of the Optune on the same basis. There was no other basis for the denial and the medical evidence relating to Appellant and her need or eligibility for treatment was not discussed in the denials. Appellant timely filed a timely request for a hearing before an Administrative Law Judge (ALJ) and the amount in controversy meets the jurisdictional requirement for this action. *See* 42 C.F.R. §§ 405.1006 and 422.600(b).

The evidence in the record indicates that Optune is a portable, wearable medical device that delivers TTFT to a targeted tumor. On April 8, 2011, the U.S. Food and Drug Administration (FDA) approved TTFT for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy and as an alternative to standard medical therapy for glioblastoma multiforme after surgical and radiation options have been exhausted.

In 2015, Optune received additional pre-market approval from the FDA for newly diagnosed glioblastoma in combination with Temozolomide after standard surgical resection and radiation therapy. The Provider is the sole global supplier for the Optune System and they are currently out-of-network for the Plan. Therefore, the treatment is appropriate for both newly diagnosed

and recurrent glioblastoma. The evidence is un rebutted in the medical record that Appellant is eligible for the FDA approved treatment.

Pursuant to proper notice, Appellant's telephonic hearing was scheduled for March 1, 2018. Hearing notice was mailed January 19, 2017. The Plan nor the IRE responded to the notice, nor did either timely submit additional evidence. Pursuant to 42 C.F.R. Sec. 405.1000(g) and 42 C.F.R. Sec. 405.1038(a), the undersigned finds the evidence in the medical record supports a fully favorable decision. Therefore, the undersigned decides this case on the record and the hearing scheduled for March 1, 2018 is vacated.

All Exhibits are admitted into evidence on the record and the undersigned provides excerpts at Exhibit 5, for items he has taken administrative notice of. In this regard, the undersigned takes administrative notice of certain medical literature documents pertaining to TTFT, which are contained on the Novocare website, including medical literature from 2016-present that has greatly adopted the Optune treatment and are supported by numerous clinical studies which establish improved survival rates using the Optune treatment. Moreover, the undersigned finds this recent medical literature supersedes all medical literature which the LCD relied upon at the time.

Furthermore, the undersigned takes administrative notice of the applicable LCD, L34823 and citations to authority, and Medicare Appeals Council (MAC) decision M-15-1354, which involved TTFT, and numerous Novocare press releases which established multiple health plans and nations such as Australia and Japan, now offer Optune coverage as a treatment. One article observing Anthem's positive coverage of Optune touts that more than 97 million Americans are now covered for Optune. Additionally, the undersigned takes administrative notice of recent publications including but not limited to: the *Journal of American Medical Association* (Stupp & Kanner); the *Annual Meeting of the American Association for Cancer Research* (Stupp); and the *World Journal of Surgical Oncology* (Chaudhry, Benson, & Varshaver), amongst others, which reflect positive recommendations for the treatment. These peer review publications tout a significant increase in survival rates using the Optune system in conjunction with Temozolomide for newly diagnosed glioblastoma.¹

Issues

Whether the Plan is required to cover the TTFT (Optune) and whether an out-of-network exception should be granted, if applicable?

Relevant Facts in the Record

The record indicates Appellant, a 77 year old female, requested the Plan to pre-approve coverage for Optune Plus Transducers to treat her glioblastoma. (Exh. 2). Appellant had suffered a seizure on August 23, 2017. She underwent a CT scan of the brain which showed a tumor located in the right anterior frontal lobe with extension into the corpus callosum crossing midline with surrounding edema. She then underwent magnetic resonance imaging (MRI) on August 24,

¹ Blue Cross Blue Shield of Michigan, Japan, Australia, Anthem, and Humana have authorized coverage for the Optune treatment. A news release dated March 3, 2016, observes Humana accepted Optune treatment. A June 5, 2017 article indicates Health Care Service Corporation will now cover Optune. (See Exhibit 5, excerpts).

2017 and the MRI was consistent, showing a 2.9 times 1.8 times 2.1 cm peripherally enhancing mass with surrounding edema. A Brainlab guided biopsy was performed on August 29, 2017 which was reviewed by the Cleveland Clinic, where she had a consultation. Pathology reports confirmed the brain cancer, consistent with "GBM, WHO grade IV (glioblastoma multiforme). (Exh. 2). The treating doctors at Arizona Oncology has prescribed the best course of treatment as being the Optune System in combination with Temozolomide, which according to her treating doctor, Dr. M.D, is medically necessary. (Exh. 2, at 7-9). Additional excision is not recommended due to the location of the tumor. She completed radiotherapy and the treating doctor opines that Optune treatment is her next and best course of treatment. Dr. highly recommends the Optune treatment and opines it is medically reasonable and necessary for Appellant. The record includes a detailed letter of medical necessity written by Dr. which the undersigned finds is highly probative. (Exh. 2, at 7-9).

In addition to the articles described above, the medical record indicates that over 180 health plan payers, including Humana Health, have covered this therapy for certain members after an appeal process. Dr. also indicated that Optune with Temozolomide is now a National Comprehensive Cancer Network (NCCN) positive Category 2A recommendation following postoperative standard brain radiation therapy with concurrent Temozolomide, meaning the NCCN has recently upgraded its recommendation for the Optune treatment. Given the aggressive nature and extremely limited treatment options of Appellant's disease, Dr. Vonk strongly recommends Appellant receive coverage for Optune, as soon as possible. (Exh. 2, at 7-9).

The medical record also establishes that FDA approved Optune in April 2011 for recurrent glioblastoma, based on the results of a large clinical trial that showed that treatment with Optune delivered comparable overall survival and progression free survival (PFS) to chemotherapy with minimal toxicity and an improvement in patients' quality of life compared to chemotherapy. Dr. Vonk further explained that FDA approval in 2015 for Optune for newly diagnosed glioblastoma in combination with Temozolomide was based on a prospective, randomized, open label, active parallel control trial to compare the effectiveness and safety outcomes of newly diagnosed glioblastoma multiforme patients treated with Optune and Temozolomide to those treated with Temozolomide alone. The results of the trial at the interim analysis showed superior efficacy both in PFS as well as overall survival. Dr. indicated that the data was so compelling that the independent data monitoring committee recommended the trial be terminated so that patients in the standard of care arm could cross over. The FDA approved the supplemental IDE to allow for crossover of patients on the control arm to the TTFT arm on December 1, 2014. (Exh. 2, at 7-9).

The pre-specified interim analysis of the trial data was conducted on the first 315 patients, representing approximately 50 percent of the targeted study population. The data showed that patients treated with TTFT together with Temozolomide demonstrated a significant increase in PFS compared to Temozolomide alone (PFS of 7.1 months compared to 4.0 months). Patients treated with TTFT together with Temozolomide demonstrated a significant increase in overall survival compared to Temozolomide alone (overall survival of 19.6 months compared to 16.6 months). Additionally, the percentage of patients alive at 2 years with TTFT together with Temozolomide was 43% compared to the 29% of patients using Temozolomide alone. (Exh. 2).

There is no issue that Appellant is medically cleared and qualifies for the Optune treatment. Dr. confirms this.

The record indicates a copy of the Plan's Evidence of Coverage appears in a CD, but no such CD was forwarded to this appeal level.

In this case, Appellant requests approval of the Optune treatment and approval for an out-of-network exception, if applicable so that Appellant can access Optune under her network benefits.

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an adverse organization determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act (Act) § 1859(g)(5); *see* 42 C.F.R. § 422.600. The request for hearing is timely filed if filed within 60 days of the date of notice of a reconsidered determination. 42 C.F.R. § 422.602.

In implementing this statutory directive, the Secretary delegated authority to administer the nationwide hearings and appeals system for the Medicare program to the Office of Medicare Hearings and Appeals (OMHA). *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

B. Scope of Review

Medicare Advantage Organization determinations and appeals are governed by the regulations in 42 C.F.R. §§ 422.560 through 422.626. Unless otherwise noted, the ALJ hearing procedures set forth in 42 C.F.R. §§ 405.1000 through 405.1064 apply to Medicare Advantage appeals, to the extent they are appropriate. 42 C.F.R. § 422.562(d).

The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. 42 C.F.R. § 405.1032(a). However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, he or she may notify the parties before the hearing and may consider it an issue at the hearing. *Id.*

C. Standard of Review

OMHA is staffed with ALJs who conduct *de novo* hearings. 42 C.F.R. § 405.1000(d). A *de novo* review means the ALJ reviews the evidence without regard to the findings in the prior determinations on the claim and makes an independent assessment based on the evidence and the controlling laws. However, the burden of proving each element of a Medicare claim lies with the appellant and is satisfied by submitting sufficient evidence in accordance with Medicare rules. *See e.g.*, Act §§ 1814(a)(1), 1815(b), and 1833(e); *see also* 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, and 405.1030.

II. Principles of Law

A. Statutes and Regulations

Eligibility for Medicare benefits is determined under Title XVIII of the Act, 42 U.S.C. § 1801 et seq., and federal regulations set forth in Title 42 of the Code of Federal Regulations.

The Medicare Part C program establishes standards and sets forth the requirements, limitations, and procedures for Medicare services furnished, or paid for, by Medicare Advantage (MA) organizations through MA plans. *See* Act § 1851 *et seq.*; *see also* 42 C.F.R. § 422.1(b) *et seq.* A person is eligible to enroll in Part C if s/he is entitled to Medicare Part A and enrolled in Part B; has not been medically determined to have end-stage renal disease; and meets the applicable residency requirements. *See* Act § 1851(a)(3) – (b); *see also* 42 C.F.R. § 422.50(a).

Generally, an MA plan must provide coverage of, by furnishing, arranging for, or making payment for, all services that are covered by Parts A and B of Medicare (Original Medicare) and available to beneficiaries residing in the plan's service area. *See* Act § 1852(a)(1); *see also* 42 C.F.R. § 422.101(a). The MAO must disclose the benefits offered under the MA plan, including applicable conditions and limitations, premiums and cost sharing (such as copayments, deductibles, and coinsurance), and any other conditions associated with receipt or use of benefits. 42 C.F.R. § 422.111.

According to section 1862(a)(1)(A) of the Act, no payment may be made under Original Medicare for any expenses incurred for items or services that are “not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *See* 42 U.S.C. § 1395y(a)(1)(A); *see also* 42 C.F.R. § 411.15(k)(1).

B. Policy and Guidance

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination (NCD), can establish or change a substantive legal standard governing the scope of the benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. NCDs promulgated by the Secretary of HHS under the authority of Section 1862(a)(1) of the Act dictate the criteria under which Medicare covers specified services, procedures or supplies. NCDs are binding upon ALJs. 42 C.F.R. § 405.1060(a)(4); *see* 42 C.F.R. § 405.1060(b)(1) (“An ALJ may not disregard, set aside or otherwise review an NCD”).

Although not subject to the force and effect of law, CMS and its contractors issue policies, manuals and guidelines that describe criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (LCDs). **42 C.F.R. § 405.1062 states that an ALJ is not bound by LCDs or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect.** (emphasis added).

LCD L34823 entitled “Tumor Treatment Field Therapy (TTFT)” provides that TTFT (E0766) will be denied as not reasonable and necessary.

The undersigned notes that the LCD contains a blanket citation to authorities for support but provides no rationale, discussion or criteria upon which exceptions can be made within the context of the LCD, or upon which the LCD is based. A closer look at the relied upon citations in the LCD are outdated and do not take into account recent studies and the medical community’s acceptance of the Optune treatment, which has greatly expanded over the last two years. Moreover, it does not discuss what authorities it specifically relies upon, nor what the authorities purport to state. This is significant as will be discussed more fully below.

Moreover, Medicare Policy Article A52711 provides additional guidance for TTFT, and seems to provide some inconsistent analysis with the LCD, which purports to allow coverage where appropriate and states, as follows:

NON-MEDICAL NECESSITY COVERAGE AND PAYMENT RULES:

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements.

Information provided in this policy article relates to determinations other than those based on Social Security Act §1862(a)(1)(A) provisions (i.e. “reasonable and necessary”). **Tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act §1861(s)(6)).** In order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met. In addition, there are specific statutory payment policy requirements, discussed below, that also must be met.

Code E0766 is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling.

Code A4555 is not valid for billing to Medicare. If code A4555 is billed, it will be denied as an invalid code.

CODING GUIDELINES

Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers.

This code is inclusive of all associated supplies necessary for the effective use of code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

Suppliers should contact the Pricing, Data Analysis and Coding (PDAC) Contractor for guidance on the correct coding of these items.

The accompanying Policy Article A52711 therefore establishes that TTFT is categorized under the Durable Medical Equipment benefit. The article explains that code E0766 describes “devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers.” The article further states that TTFT devices are in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. While it defers to any applicable LCD it confirms categorically that in particular medical cases such treatments should be found to be medically reasonable and necessary. Additionally, it anticipates that any applicable LCD will provide eligibility criteria and not be a blanket denial for all cases.

Analysis

After careful consideration of the evidence the undersigned finds that the Optune treatment is medically reasonable and necessary for purposes of coverage under Medicare, and that out-of-network coverage is warranted, if applicable, for this particular Appellant. The aforementioned policy letter and the underlying analysis that went into it clearly anticipate that there are medical situations where the Optune treatment would be medically reasonable and necessary, and it can be approved as a Part B DME. While it ultimately defers to any LCD which may be applicable, clearly the policy letter provides policy support that the treatment has merit and may qualify as a covered DME under the Act, in appropriate medical situations. This case is an appropriate medical situation.

The undersigned finds the extensive medical evidence in the record overwhelmingly supports coverage. The medical evidence establishes the Optune treatment is medically reasonable and necessary for Appellant. That evidence starts with her treating doctor, Dr. [redacted] whose medical opinions are deemed highly probative. Appellant has carried her burden of proof. This evidence includes the letter of medical necessity by the treating physician, as well as the Cleveland Clinic Consultation and the extensive treatment records, confirming her diagnosis, and medical eligibility to be treated with the Optune system. Furthermore, the medical record indicates that further excision is not an option for Appellant. The only option now since already undergoing radiotherapy is the Optune treatment, in combination with Temozolomide. The evidence submitted in the file by Dr. [redacted] and Novocure including the upgraded recent recommendations for use by the NCCN, is highly probative. Medical literature overwhelmingly supports treatment by Optune in patients like Appellant. The Optune treatment is well accepted in the medical community and is often the last viable resort for glioblastoma patients.

It is also probative and un-rebutted that over 180 health insurers, reaching over 97 million Americans have allowed coverage in appropriate cases. The medical evidence establishes Appellant’s case is an appropriate case for this treatment. (Exhibit 5, excerpts).

To be clear, this appeal addresses whether the Plan is required to cover the Optune treatment at issue, to this particular Appellant. The IRE concluded that the Plan did not have to provide pre-approval for the device based on LCD L34823 that states that TTFT will be denied as not reasonable and necessary. No further rationale is provided and it is un-rebutted that the Optune treatment is medically necessary for the Appellant. The undersigned further finds the application of the LCD is void of any rationale or discussion and the LCD merely cites certain authorities, which on their face, are outdated, and cannot be relied upon in this case, and which do not address the most recent studies, and more recent acceptance of the treatment by numerous health plans, as well as the NCCN positive recommendation for using the Optune treatment. While giving due consideration to the LCD the undersigned finds the LCD should **NOT** be followed in this case.

In weighing the medical evidence and giving due consideration to the LCD, the undersigned finds the extensive medical evidence in the record establishes the Optune treatment in all medical probability will greatly enhance the life span of Appellant. The Plan has provided no medical evidence in the record to cast any doubt about the effectiveness of the treatment, especially as applied to the Appellant. The decision by the Plan and affirmance by the IRE, is based solely upon the LCD general prohibition, and provides no medical analysis of Appellant's medical diagnosis or condition. The denial decisions further ignore the great weight of medical literature and the NCCN recommendation that establishes the Optune treatment is now readily accepted in the medical community. Dr. [redacted] has indicated that the requested treatment in this case is medically necessary and reasonable and that Appellant meets the standards for FDA approved treatment, and this evidence is unrebutted.

Further, the Plan does not contain any explanation for how it reached its denial conclusion, nor does the LCD explain its conclusion for providing no exception criteria. The undersigned finds the LCD provides no meaningful rationale to justify blanket denials for the Optune treatment and that it is inconsistent with the aforementioned agency policy letter on this subject. The LCD if applied must be read in conjunction with the policy letter in a common sense manner and allow coverage where medically necessary and reasonable. It is quite a paradox for over 97 million Americans (which includes coverage by Humana health) to now have coverage for the Optune system, yet Medicare will deny coverage?

The undersigned finds that Federal regulations permit an ALJ to decline to follow a local coverage policy in an individual case. 42 C.F.R. Sec. 405.1062. The undersigned therefore has considered, yet declines to defer to LCD L34823 in this case, based upon the medical record.

The undersigned recognizes there is an older MAC decision which reversed one ALJ decision pertaining to TTFT, although this may be an anomaly since the record indicates there are several ALJ decisions in favor for Optune treatment which have apparently not been reversed, as well as a policy letter by the Agency and overwhelming medical literature which recognizes the treatment is effective when used according to FDA approved purposes. In any event, the undersigned finds that case is distinguishable, and the holding in that decision is outdated.

That case, M-15-1534, focused on what it perceived as the ALJ decision striking down the entire LCD. The result in that MAC decision also relied heavily upon the citation to authorities in the LCD, presumably to reach its conclusion that there was some doubt at the time the LCD was enacted, about the effectiveness of the Optune treatment within the medical community. Based upon that record, the MAC found an insufficient medical record was established to support the

ALJ's decision not to defer to the LCD. Certainly, this case and the undersigned's decision herein does not involve a challenge to the LCD (pursuant to Part 426 or otherwise), and the legal stature of the LCD is not an issue here.²

While the LCD validity is not at issue in this case, it is appropriate for the undersigned to analyze any perceived deficiencies in the LCD and its rationale, the current state of the medical community's view of the Optune treatment, and the current validity of the underlying sources cited in the LCD, otherwise the undersigned would never know when to defer or not defer to follow the LCD. In this regard, it is noteworthy that the MAC decision is already over two years old. During 2016 and 2017, the medical community has favorably embraced the Optune treatment. Moreover, the evidence in the record establishes the authorities the LCD relied upon, are now outdated and do not necessarily reflect the consensus of the medical community, especially in light of recent advances and consensus by numerous Plans to cover Optune. (Exh. 5; Exh. 2, at 7-9).

In this context, the sparse nature of any medical reasoning in the LCD provides additional reasons not to follow it here, where the medical evidence in this record is so overwhelming that

² The MAC decision also criticizes the deciding ALJ decision it reversed indicating the decision did not explain the significance of the various medical literature which was admitted into evidence to support the premise that the Optune treatment is effective. The MAC decision infers the medical evidence in that case relied solely upon this medical literature. That is not the situation here. The letter of medical necessity and clinical notes by the treating doctor, in addition to the medical literature and new studies and clinical trials, as well as evidence that a significant number of medical insurance payers now provide coverage for Optune, establish the medical community accepts Optune as a break-through brain cancer treatment. Moreover, the MAC decision indicates in its last paragraph that the LCD will eventually be updated if warranted and if the medical literature substantially establishes the validity of the treatment. However, circumstances have changed since issuance of that decision. The MAC decision was decided over two years ago and the underlying evidentiary record in the ALJ decision goes back even further. The LCD has not been substantially revised towards coverage nor has it addressed the significant medical advances of the Optune treatment. Additionally, the undersigned finds the sources cited in the LCD are outdated and that subsequent revision were in essence pro forma only. Indeed, it appears as though not all of the old sources cited in the LCD even reach the consensus conclusion in the LCD as two of the cited sources cite to the Novocure website and Novocure's safety summary, and a third cites to a Novocure sponsored study, cite source 7, as reflected and commented upon in cite source 11. This source 11 was published by the Australian Government and published in 2009, which pre-dates even FDA approval of Optune. It in fact notes some survival rates based upon two small studies and recommends monitoring the effectiveness of Optune over a 24 month period. In any event, on their face, the citation dates for each source cited in the LCD establishes that they have not been updated. Appellant has no time to await future administrative revisions. It is clear that the LCD has not kept pace with the medical technology and literature, and the LCD cannot be relied upon in this particular case to deny the treatment to Appellant, where all of the admitted medical evidence in this record supports a finding that the treatment is medically reasonable and necessary for this Appellant at this time. It is clear that the treatment has worked for many patients and has been approved by various medical plans in particular cases, and will in all medical probability be successful for Appellant.

in this Appellant's case, the Optune treatment is more likely than not, going to increase her life span survival. It is also significant that since the MAC case was decided additional studies have proven the effectiveness of the Optune treatment during this period, and by the change of position in many medical insurance entities. In the Novocure press releases and website it confirms that additional tens of millions of plan members are now covered for Optune. This adds to positive coverage from such health entities as Anthem, Regence BCBS, Preferred One, Univera Healthcare, Asuris Northwest Health, and Group Health Cooperative Washington and Idaho.

Moreover, a BCBS article, *BCN Provider News* provides: "The safety and effectiveness of TTF therapy is established for the treatment of supratentorial glioblastoma. TTF therapy may be medically necessary when used under the care of a physician, in adults 22 years and older and as an adjunct therapy to standard therapy." (Exh. 5).

Under the regulations, which unlike policy, has the force and effect of law, the undersigned ALJ has the authority to carefully consider the LCD and then elect to depart from it based upon the evidentiary record. Here, the medical evidence in the administrative record supports the finding that for Appellant the Optune treatment is medically reasonable and necessary for this Appellant, at this time.

The Optune treatment has dramatically expanded survival rates for the type of aggressive brain cancer from which Appellant suffers from. The data showed that patients treated with TTFT together with Temozolomide demonstrated a PFS of 7.1 months compared to 4.0 months for patients treated with Temozolomide alone. Patients treated with TTFT together with Temozolomide also demonstrated a significant increase in overall survival compared to Temozolomide alone (overall survival of 19.6 months compared to 16.6 months). The LCD has not been recently updated substantively and therefore does not consider or address these recent break-through results or general acceptance consensus from the medical community and accordingly the undersigned will not defer to it in this particular case. (Exh. 2).

The undersigned therefore finds that the TTFT device known as Optune, is medically reasonable and necessary for Appellant. In addition, the Provider is entitled to an in-network exception if there are no in-network providers of the device. The medical record contains sufficient documentation of Appellant's disease to substantiate the medical reasonableness and necessity for the Optune treatment at issue, satisfying Medicare rules and regulations.

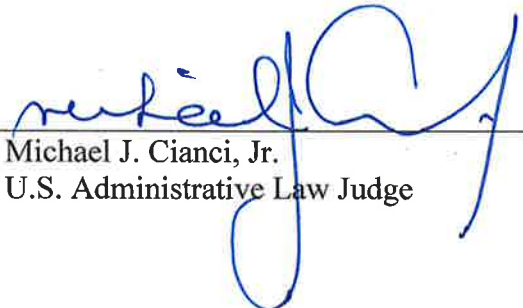
Conclusions of Law and Order

For the reasons above, the Plan and/or its affiliates, is required to provide coverage for the Optune treatment, including if applicable and necessary an out-of-network provider exception.

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: FEB 14 2018


Michael J. Cianci, Jr.
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Irvine Field Office
Irvine, CA

Appeal of:	ALJ Appeal No.: 1-5366320223
Beneficiary:	Medicare: Part C [EXPEDITED]
HICN: ***.**4424A	Before: Michael Ciani U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented, a **FULLY FAVORABLE** decision is entered for (Appellant).

Procedural History

Appellant requested Blue Cross Blue Shield of Western New York (BCBS) to pre-approve coverage for an electrical stimulation device used for cancer treatment (HCPCS E0766). The tumor treatment field therapy (TTFT) called Optune, is supplied by Novocure, Inc. (Provider). BCBS denied the pre-approval initially and on appeal, on the basis that a Local Coverage Determination (LCD) (L34823) precludes payment. The LCD states TTFT treatments are not medically reasonable and necessary. Independent Review Entity MAXIMUS Federal Services (the IRE) also denied pre-approval of the Optune on the same basis. Appellant timely filed a request for a hearing before an Administrative Law Judge (ALJ) and the amount in controversy meets the jurisdictional requirement for this action. *See* 42 C.F.R. §§ 405.1006 and 422.600(b).

The evidence in the record indicates that Optune is a portable, wearable medical device that delivers TTFT to a targeted tumor. On April 8, 2011, the U.S. Food and Drug Administration (FDA) approved TTFT for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy and as an alternative to standard medical therapy for glioblastoma multiforme after surgical and radiation options have been exhausted.

In 2015, Optune received additional pre-market approval from the FDA for newly diagnosed glioblastoma in combination with Temozolomide after standard surgical resection and radiation therapy. The Provider is the sole global supplier for the Optune System and they are currently out-of-network with BCBS.

Pursuant to proper notice, Appellant's telephonic hearing was conducted on December 8, 2016. Appointed Representative from Novocure Mr. Dan McCoy, Health Policy Analyst, appeared for Appellant and provided testimony. BCBS timely elected to appear as a party through Legal Counsel Ms. Tammy Riddle with testimony by Ms. Cinnamon Radke, Grievance and Appeal Specialist, and Medical Director Dr. Alan Saltzman, M.D.

Exhibits 1 through 4 were admitted into the record without objection. Additionally, the undersigned took administrative notice of two medical literature documents pertaining to TTFT, one by Group Health, referred to as a Clinical Review Criteria, and the other by Health Net, Policy number NMP523 updated May 2016. Both summarize recent Optune uses and clinical studies and note improved survival rates using the Optune treatment. Excerpts were attached to the record. Furthermore, the undersigned took administrative notice of the applicable LCD, L34823 and citations to authority, and Medicare Appeals Council (MAC) decision M-15-1354, which involved TTFT, and a recent Novocure press release which announced that as of May 4, 2016, BCBS of Michigan would offer Optune coverage as a treatment, excerpts also attached. Appellant's representative knowingly and voluntarily waived right to counsel.

Issues

Whether BCBS is required to cover the TTFT (Optune) and whether an out-of-network exception should be granted?

Relevant Facts in the Record

The record indicates Appellant requested BCBS to pre-approve coverage for Optune Plus Transducers to treat glioblastoma multiforme. Appellant has a history of a right cerebellopontine angle meningioma for which he underwent gamma knife radiosurgery. (Exh. 1 at 25-26, 99-101; Exh. 2 at 5). Appellant had suffered a grand mal seizure on June 20, 2016. He underwent magnetic resonance imaging (MRI) the same day and the MRI was consistent with the meningioma he and his physician were aware of but it also showed a 2.5 cm mass in the right parietal convexity. Biopsy confirmed glioblastoma multiforme. Appellant completed an adjuvant course of radiotherapy for his right parietal convexity glioblastoma. He was treated by his physician, Dr. Dhiren Shah, in adjuvant fashion from July 25, 2016 to September 19, 2016 in 32 fractions over 44 elapsed days. Treatments were initially delivered to the edema then continued to the tumor bed. Appellant received concurrent Temozolomide with his radiation. Appellant underwent MRI on October 6, 2016 which Dr. Shah reviewed. It showed an area of enhancement at the original resection cavity. After discussing treatment options with Appellant, Dr. Shah decided that Optune would be the best therapy for Appellant. Dr. Shah highly recommends the Optune treatment and opines it is medically reasonable and necessary for Appellant.

The record includes a letter of medical necessity written by Dr. Shah at Exh. 1 at 99-101 in which he requests a network exception for Appellant because there is no provider in the BCBS of Western New York network who can provide Optune. Dr. Shah noted that over 180 payers, including BCBS of Western New York, have covered this therapy for certain members after an appeal process. Dr. Shah also indicated that Optune with Temozolomide is now a National Comprehensive Cancer Network (NCCN) Category 2A recommendation following postoperative standard brain radiation therapy with concurrent Temozolomide, meaning the NCCN has recently upgraded its recommendation for the Optune treatment. Given the aggressive nature

and extremely limited treatment options of Appellant's disease, Dr. Shah strongly recommends Appellant receive coverage for Optune.

Dr. Shah indicated that FDA approval for Optune in April 2011 for recurrent glioblastoma was based on the results of a large clinical trial that showed that treatment with Optune delivered comparable overall survival and progression free survival (PFS) to chemotherapy with minimal toxicity and an improvement in patients' quality of life compared to chemotherapy. Dr. Shah further explained that FDA approval in 2015 for Optune for newly diagnosed glioblastoma in combination with Temozolomide was based on a prospective, randomized, open label, active parallel control trial to compare the effectiveness and safety outcomes of newly diagnosed glioblastoma multiforme patients treated with Optune and Temozolomide to those treated with Temozolomide alone. The results of the trial at the interim analysis showed superior efficacy both in PFS as well as overall survival. Dr. Shah indicated that the data was so compelling that the independent data monitoring committee recommended the trial be terminated so that patients in the standard of care arm could cross over. The FDA approved the supplemental IDE to allow for crossover of patients on the control arm to the TTFT arm on December 1, 2014. (Exh. 1 at 99-101 & Hearing Record, McCoy).

The pre-specified interim analysis of the trial data was conducted on the first 315 patients, representing approximately 50 percent of the targeted study population. The data showed that patients treated with TTFT together with Temozolomide demonstrated a significant increase in PFS compared to Temozolomide alone (PFS of 7.1 months compared to 4.0 months). Patients treated with TTFT together with Temozolomide demonstrated a significant increase in overall survival compared to Temozolomide alone (overall survival of 19.6 months compared to 16.6 months). Additionally, the percentage of patients alive at 2 years with TTFT together with Temozolomide was 43% compared to the 29% of patients using Temozolomide alone.

Mr. McCoy of Novocure testified for Appellant requesting the undersigned to approve coverage for Appellant. As Dr. Shah indicated in his letter of medical necessity, Mr. McCoy testified that Novocure received FDA approval in October 2015 for newly diagnosed glioblastoma in combination with Temozolomide based on a large clinical trial that showed superior efficacy in survival for patients using Optune with Temozolomide compared to Temozolomide alone. He also stated that the trial was terminated early in order to begin treating patients with Optune in conjunction with Temozolomide. Mr. McCoy indicated that Optune treatment statistically speaking provides patients with a forty eight percent survival rate over two years compared to thirty two percent for Temozolomide alone. He also testified that Optune with Temozolomide is now an NCCN Category 2A recommendation following postoperative standard brain radiation therapy with concurrent Temozolomide. Mr. McCoy stated that Category 2A recommendations have uniform consensus among the medical panel as being medically reasonable and necessary and being the standard of care for treating glioblastoma. He also stated that he is aware of multiple medical insurance payer entities that cover Optune, which in his view necessarily means the treatment is viewed in the medical community as being medically reasonable and necessary. Additionally, he noted peer consensus at a recent formal meeting of the Society of Neurology & Oncology, opining that the Optune treatment has been the break-through treatment in the last ten years for this type of brain cancer. Mr. McCoy testified that the LCD applicable here, which has been used as the mechanism to deny Optune to Appellant, contains only those outdated citations to authorities which have not been updated and do not incorporate the recent successful clinical trials and studies Optune has had over the last year. (Hearing Record; See Exh.1 at 37-49 for some notable clinical trial summaries and results).

There is no issue that Appellant is medically cleared and qualifies for the Optune treatment. Dr. Saltzman also confirms this in response to questions from the undersigned, acknowledging that Appellant qualifies for the FDA approved uses for the Optune treatment. (Hearing Record).

Ms. Radke testified for the Plan and indicated the Plan's position was still essentially the same, that is, since Original Medicare would not provide coverage on the basis of the LCD, it would not. Ms. Radke testified that the Plan does not review the accuracy of LCDs. She had no knowledge of any medical evidence in the record which would not otherwise support a conclusion that Optune was not medically reasonable and necessary in this case. She noted the Plan's insurance protocol that appears in the record, is likewise in accord with Medicare, but upon questioning by the undersigned acknowledged that the protocol states a new revision was due in September 2016; she did not know the status of the revision or whether any changes had been made in light of new studies favoring the use of the Optune treatment.

Dr. Saltzman also testified for the Plan, indicating that policies for BCBS plans are in general independently developed, although there is some policy coordination between Plans within the BCBS association. The undersigned finds this significant in light of recent decisions by BCBS and announcements that some of its Plans are covering the Optune treatment. Dr. Saltzman also stated in response to some questions by the undersigned that although he has some questions regarding some of the new trial studies success, he did not view Appellant's request for treatment with the Optune as being unreasonable in this particular case. He believes that the Plan is obligated to follow the LCD initially. Dr. Saltzman acknowledged that Optune is FDA approved. As indicated, he testified that the requested treatment in this case is not unreasonable and that Appellant meets the FDA approved treatment, as it is not being used off label.

A copy of the Plan's Evidence of Coverage appears in the record at Exh. 1 at 327-606. The Plan is described as Forever Blue Medicare and is a PPO plan. The undersigned finds some significance to the language in the Plan which states in the coverage chart and body of the contract at Exh. 1 at 451 for 2016 coverage options and which provides a specific exception to allow coverage (for otherwise non-covered treatments even if Medicare does not cover the treatments). The language in the Plan states: "Services considered not reasonable and necessary according to the standards of Original Medicare" are not covered unless these services are found upon appeal to be a medical service that should be paid or covered because of a patient's specific situation.

In this case, Appellant requests approval of the Optune treatment and approval for an out-of-network exception so that Appellant can access Optune under his network benefits.

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an adverse organization determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act (Act) § 1859(g)(5); *see* 42

C.F.R. § 422.600. The request for hearing is timely filed if filed within 60 days of the date of notice of a reconsidered determination. 42 C.F.R. § 422.602.

In implementing this statutory directive, the Secretary delegated authority to administer the nationwide hearings and appeals system for the Medicare program to the Office of Medicare Hearings and Appeals (OMHA). *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

B. Scope of Review

Medicare Advantage Organization determinations and appeals are governed by the regulations in 42 C.F.R. §§ 422.560 through 422.626. Unless otherwise noted, the ALJ hearing procedures set forth in 42 C.F.R. §§ 405.1000 through 405.1064 apply to Medicare Advantage appeals, to the extent they are appropriate. 42 C.F.R. § 422.562(d).

The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. 42 C.F.R. § 405.1032(a). However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, he or she may notify the parties before the hearing and may consider it an issue at the hearing. *Id.*

C. Standard of Review

OMHA is staffed with ALJs who conduct *de novo* hearings. 42 C.F.R. § 405.1000(d). A *de novo* review means the ALJ reviews the evidence without regard to the findings in the prior determinations on the claim and makes an independent assessment based on the evidence and the controlling laws. However, the burden of proving each element of a Medicare claim lies with the appellant and is satisfied by submitting sufficient evidence in accordance with Medicare rules. *See e.g.*, Act §§ 1814(a)(1), 1815(b), and 1833(e); *see also* 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, and 405.1030.

II. Principles of Law

A. Statutes and Regulations

Eligibility for Medicare benefits is determined under Title XVIII of the Act, 42 U.S.C. § 1801 et seq., and federal regulations set forth in Title 42 of the Code of Federal Regulations.

The Medicare Part C program establishes standards and sets forth the requirements, limitations, and procedures for Medicare services furnished, or paid for, by Medicare Advantage (MA) organizations through MA plans. *See* Act § 1851 et seq.; *see also* 42 C.F.R. § 422.1(b) et seq. A person is eligible to enroll in Part C if s/he is entitled to Medicare Part A and enrolled in Part B; has not been medically determined to have end-stage renal disease; and meets the applicable residency requirements. *See* Act § 1851(a)(3) – (b); *see also* 42 C.F.R. § 422.50(a).

Generally, an MA plan must provide coverage of, by furnishing, arranging for, or making payment for, all services that are covered by Parts A and B of Medicare (Original Medicare) and available to beneficiaries residing in the plan's service area. *See* Act § 1852(a)(1); *see also* 42

C.F.R. § 422.101(a). The MAO must disclose the benefits offered under the MA plan, including applicable conditions and limitations, premiums and cost sharing (such as copayments, deductibles, and coinsurance), and any other conditions associated with receipt or use of benefits. 42 C.F.R. § 422.111.

According to section 1862(a)(1)(A) of the Act, no payment may be made under Original Medicare for any expenses incurred for items or services that are “not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” See 42 U.S.C. § 1395y(a)(1)(A); see also 42 C.F.R. § 411.15(k)(1).

B. Policy and Guidance

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination (NCD), can establish or change a substantive legal standard governing the scope of the benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. NCDs promulgated by the Secretary of HHS under the authority of Section 1862(a)(1) of the Act dictate the criteria under which Medicare covers specified services, procedures or supplies. NCDs are binding upon ALJs. 42 C.F.R. § 405.1060(a)(4); see 42 C.F.R. § 405.1060(b)(1) (“An ALJ may not disregard, set aside or otherwise review an NCD”).

Although not subject to the force and effect of law, CMS and its contractors issue policies, manuals and guidelines that describe criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (LCDs). **42 C.F.R. § 405.1062 states that an ALJ is not bound by LCDs or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect.** (emphasis added).

LCD L34823 entitled “Tumor Treatment Field Therapy (TTFT)” provides that TTFT (E0766) will be denied as not reasonable and necessary.

The undersigned notes that the LCD contains a blanket citation to authorities for support but provides no rationale, discussion or criteria upon which exceptions can be made within the context of the LCD, or upon which the LCD is based. Moreover, it does not discuss what authorities it specifically relies upon, nor what the authorities purport to state.

Policy Article A52711 provides additional guidance for TTFT, and seems to provide some inconsistent analysis with the LCD, as follows:

NON-MEDICAL NECESSITY COVERAGE AND PAYMENT RULES:

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements.

Information provided in this policy article relates to determinations other than those based on Social Security Act §1862(a)(1)(A) provisions (i.e. “reasonable and necessary”). **Tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act §1861(s)(6)).** In order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met. In addition, there are specific statutory payment policy requirements, discussed below, that also must be met.

Code E0766 is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling.

Code A4555 is not valid for billing to Medicare. If code A4555 is billed, it will be denied as an invalid code.

CODING GUIDELINES

Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers.

This code is inclusive of all associated supplies necessary for the effective use of code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

Suppliers should contact the Pricing, Data Analysis and Coding (PDAC) Contractor for guidance on the correct coding of these items.

The accompanying Policy Article A52711 therefore establishes that TTFT is categorized under the Durable Medical Equipment benefit. The article explains that code E0766 describes “devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers.” The article further states that TTFT devices are in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. While it defers to any applicable LCD it seems to confirm categorically that in particular cases such treatments should be found to be medically reasonable and necessary. Additionally, it anticipates that any applicable LCD will provide eligibility criteria.

Analysis

After careful consideration of the evidence and arguments presented, the undersigned finds that the Optune treatment is reasonable and necessary for purposes of coverage under Medicare, and that out-of-network coverage is warranted. The applicable policy letter and the underlying analysis that went into it clearly anticipate that there are situations where the Optune treatment would be medically reasonable and necessary, and it can be approved as a Part B DME. While it ultimately defers to any LCD which may be applicable, clearly the policy letter provides policy

support that the treatment has merit and could qualify as a covered DME under the Act. The undersigned finds this to be significant in this case, but certainly not dispositive.

The undersigned finds the extensive medical evidence in the record to be dispositive. The medical evidence establishes the Optune treatment is medically reasonable and necessary for Appellant. That evidence starts with his treating doctor, Dr. Shah, whose testimony is found to be highly probative. Appellant has carried his burden of proof. This evidence includes the letter of medical necessity by the treating physician, Mr. McCoy's testimony, the Plan's language, and the numerous medical literature articles, and recent studies, submitted by Novocure contained in Exhs.1 and 4, including upgraded recent recommendations for use by the NCCN.

As Dr. Saltzman indicated, the BCBS association is supported by all BCBS plans. (Hearing Record). The BCBS association has its own staff for proposing all policies. However, each plan in the BCBS association creates its own independent policies that may differ from the policies set out by the BCBS association. There are plans in the BCBS association that provide coverage for Optune. Dr. Shah also noted that over 180 payers, including BCBS of Western New York, have covered this therapy for members after an appeal process. To grant coverage to millions of people covered by other BCBS Plans, but deny Appellant coverage because he is on a Medicare Plan is seemingly ludicrous, arbitrary and capricious.

In this case, the undersigned took administrative notice of a news release indicating 4.6 million Plan participants of BCBS in Michigan now are covered for the Optune treatment. In any event, regardless of the Plan's own language and coverage determinations, which seems to allow exceptions where appropriate, the undersigned declines to give substantial deference to the LCD in this case. Original Medicare should cover the treatment because the LCD is not applicable in this particular case. The extensive medical evidence in the record establishes the treatment is medically reasonable and necessary for Appellant in this case, and Dr. Saltzman's testimony is deemed probative on this point as well as he recognized that this Appellant could very probably benefit from the Optune treatment.

To be clear, this appeal addresses whether BCBS is required to cover the Optune treatment at issue, to this particular Appellant. The IRE concluded that BCBS did not have to provide pre-approval for the device based on LCD L34823 that states that TTFT will be denied as not reasonable and necessary. The LCD is void of any rationale or discussion and merely cites certain authorities, which according to Mr. McCoy and on their face, are outdated, and cannot be relied upon in this case. While giving due consideration to the LCD the undersigned finds the LCD cannot be followed in this case for a multitude of reasons.

First, the medical evidence is overwhelming and unrebutted by the Plan, that Optune is medically reasonable and necessary for Appellant. It is clear that Appellant suffers from glioblastoma multiforme, an aggressive form of brain cancer. He has had extensive treatment including radiation. He, now on the advice of his medical treating doctor, seeks coverage of the Optune treatment services furnished by Novocure. The Optune treatment is highly recommended by his doctor. Optune uses alternating electrical fields to interfere with the division of malignant cells. The electric fields treatment disrupts the rapid cell division exhibited by cancer cells. A recent medical study of a large clinical trial shows that Optune treatment had minimal risks, and combining it with the drug Temozolomide, may show even more significant overall survival by several months. (Exh. 1 at 99-101, 106-115). According to Appellant's treating doctor, with Optune patients have a forty three chance of surviving two years. Also, as Mr. McCoy testified

to, this amounts to the best break-through results for treatment of this disease in a decade. (Hearing Record).

In weighing the evidence, the undersigned has extensive medical evidence in the record establishing the Optune treatment in all medical probability could greatly enhance the life span of Appellant. The Plan has provided no medical evidence to cast any doubt about the effectiveness of the treatment, especially as applied to treating Appellant. Dr. Saltzman testified that the requested treatment in this case is not unreasonable and that Appellant meets the standards for FDA approved treatment.

Further, the Plan does not contain any explanation for how it reached its denial conclusion, nor does the LCD explain its conclusion for providing no exception criteria.

Moreover, Appellant's treating physician, Dr. Shah, prescribed Optune due to the aggressive nature and extremely limited treatment options of Appellant's disease. In support of his position, and highly probative, Dr. Shah confirmed that Optune with Temozolomide is now an NCCN Category 2A recommendation following postoperative standard brain radiation therapy with concurrent Temozolomide. As Mr. McCoy stated, Category 2A recommendations have uniform consensus among the medical panel as being medically reasonable and necessary and being the standard of care for treating glioblastoma.

Additionally, the testimony of Mr. McCoy that the LCD is outdated is very probative and the undersigned gives it great weight and as applied to this case. In his view, the LCD ignores medically relevant criteria, medical opinions, and recent studies and clinical trials, which support a finding that the Optune treatment is medically reasonable and necessary for Appellant, since it has not been substantively updated. Its recent revision merely corrected a typographical error.

Federal regulations permit an ALJ to decline to follow a local coverage policy in an individual case. 42 C.F.R. Sec. 405.1062. The undersigned therefore has considered, yet declines to defer to LCD L34823 in this case.

The medical evidence in this administrative record establishes the treatment is medically reasonable and necessary. In fact, there is no evidence to the contrary in the record.

The undersigned recognizes there is a contrary MAC decision which reversed one ALJ decision pertaining to TTFT, although this may be an anomaly since Mr. McCoy indicates several ALJ decisions have been in favor for Optune treatment and have apparently not been reversed. In any event, the undersigned finds that case is distinguishable, and the holding in that decision is now outdated.

That case, M-15-1534, focused on what it perceived as the ALJ decision striking down the entire LCD. The result in that MAC decision also relied heavily upon the citation to authorities in the LCD, presumably to reach its conclusion that there was some doubt at the time the LCD was enacted, about the effectiveness of the Optune treatment within the medical community. Based upon that record, the MAC found an insufficient medical record was established to support the ALJ's decision not to defer to the LCD. Certainly, this case and the undersigned's decision

herein does not involve a challenge to the LCD (pursuant to Part 426 or otherwise), and the legal stature of the LCD is not an issue here.¹

That being said, clearly it is appropriate for the undersigned to analyze any perceived deficiencies in the LCD and its rationale, the current state of the medical community's view of the Optune treatment, and the current validity of the underlying sources cited in the LCD, otherwise the undersigned would never know when to defer or not defer. In this regard, it is noteworthy that the MAC decision is already almost one year old. During 2016, the medical community has more favorably embraced the Optune treatment. Moreover, the evidence in the record establishes the authorities the LCD relied upon, are now outdated and do not necessarily reflect the consensus of the medical community, especially in light of recent advances and consensus by numerous Plans to cover Optune.

¹ The MAC decision also criticizes the deciding ALJ decision it reversed indicating the decision did not explain the significance of the various medical literature which was admitted into evidence to support the premise that the Optune treatment is effective. The MAC decision infers the medical evidence in that case relied solely upon this medical literature. That is not the situation here. The letter of medical necessity and clinical notes by the treating doctor and testimony by Mr. McCoy, in addition to the medical literature and new studies and clinical trials, as well as evidence that a significant number of medical insurance payers now provide coverage for Optune, establish the medical community accepts Optune as a break-through brain cancer treatment. Moreover, the MAC decision indicates in its last paragraph that the LCD will eventually be updated if warranted and if the medical literature substantially establishes the validity of the treatment. However, circumstances have changed since issuance of that decision. The MAC decision was decided almost a year ago and the underlying evidentiary record in the ALJ decision goes back even further. The LCD has not been substantially revised towards coverage nor has it addressed the significant medical advances of the Optune treatment, as indicated by Dr. Shah and testified to by Mr. McCoy. Additionally, Mr. McCoy's testimony establishes that the sources cited in the LCD are outdated and not valid, and that a July revision was in essence pro forma. Indeed, it appears as though not all of the old sources cited in the LCD even reach the consensus conclusion in the LCD as two of the cited sources cite to the Novocure website and Novocure's safety summary, and a third cites to a Novocure sponsored study, cite source 7, as reflected and commented upon in cite source 11. This source 11 was published by the Australian Government and published in 2009, which pre-dates even FDA approval of Optune. It in fact notes some survival rates based upon two small studies and recommends monitoring the effectiveness of Optune over a 24 month period. In any event, on their face, the citation dates for each source cited in the LCD corroborates Mr. McCoy's testimony that they have not been updated. Appellant has no time to await future administrative revisions. It is clear that the LCD has not kept pace with the medical technology and literature, and the LCD cannot be relied upon in this particular case to deny the treatment to Appellant, where all of the admitted medical evidence in this record supports a finding that the treatment is medically reasonable and necessary for this Appellant at this time. It is clear that the treatment has worked for many patients and has been approved by various medical institutions and entities in particular cases, and will in all medical probability be successful for Appellant. Even the Medical Director for the Plan in this case indicated Appellant's request for Optune treatment was not unreasonable under his particular facts and condition.

In this context, the sparse nature of any medical reasoning in the LCD provides additional reasons not to follow it here, where the medical evidence in this record is so overwhelming that in this Appellant's case, the Optune treatment is more likely than not, going to increase his life span survival by several months, or more. It is also significant that since the MAC case was decided additional studies have proven the effectiveness of the Optune treatment during this period, and by the change of position in many medical insurance entities. In the Novocure press dated May 4, 2016, which the undersigned took administrative notice of, it was declared that "[m]ore than 112 million Americans now have coverage of Optune as a treatment for newly diagnosed and/or recurrent glioblastoma." (Hearing Record excerpt). This adds to positive coverage from Regence BCBS, Preferred One, Univera Healthcare, Asuris Northwest Health, and Group Health Cooperative Washington and Idaho, all implemented since March 2016. (*Id.*)

Moreover, the undersigned finds Mr. McCoy's testimony probative that the authorities cited by the LCD are now largely outdated and the latest revisions to the LCD do not consider the new clinical trials and studies described by Mr. McCoy and Dr. Shah, and the accompanying medical literature in the record. For instance, citing from a BCBS article contained in the case file, *BCN Provider News*: "The safety and effectiveness of TTF therapy is established for the treatment of supratentorial glioblastoma. TTF therapy may be medically necessary when used under the care of a physician, in adults 22 years and older and as an adjunct therapy to standard therapy." (See Exh. 4; See also conclusions from *Journal of the American Medical Association* at Exh. 1 at 107). The undersigned finds the *BCN News* article moderately probative as it establishes a policy consensus among the BCBS association of a change of position, favoring coverage now.

Under the regulations, which unlike policy, has the force and effect of law, the undersigned ALJ has the authority to carefully consider the LCD and then elect to depart from it based upon the evidentiary record. Here, the medical evidence in the administrative record supports the finding that for Appellant the Optune treatment is medically reasonable and necessary for this Appellant.

In addition to research articles submitted in support of the conclusion that Optune is safe and effective in treating Appellant's condition, including the aforementioned *BCN News* excerpt, the undersigned finds the letter of medical necessity by the treating doctor, Dr. Shah (Exh. 1 at 99-101) to be highly probative. The Optune treatment has dramatically expanded survival rates for the type of aggressive brain cancer from which Appellant suffers from. The data showed that patients treated with TTFT together with Temozolomide demonstrated a PFS of 7.1 months compared to 4.0 months for patients treated with Temozolomide alone. Patients treated with TTFT together with Temozolomide also demonstrated a significant increase in overall survival compared to Temozolomide alone (overall survival of 19.6 months compared to 16.6 months). The LCD has not been recently updated substantively and therefore does not consider or address these recent break-through results or general acceptance consensus from the medical community and accordingly the undersigned will not defer to it in this particular case.

The undersigned therefore finds that the TTFT device known as Optune, is medically reasonable and necessary for Appellant. In addition, the Provider is entitled to an in-network exception because there are no in-network providers of the device. BCBS must provide supplemental coverage for the TTFT at issue. The medical record contains sufficient documentation of Appellant's disease to substantiate the medical reasonableness and necessity for the Optune treatment at issue, satisfying Medicare rules and regulations.

Conclusions of Law and Order

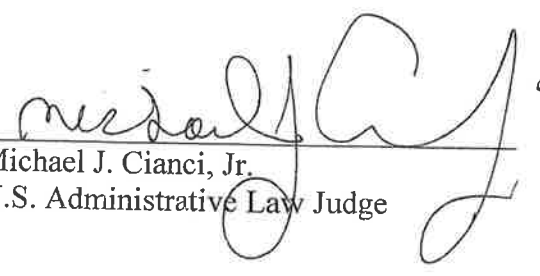
For the reasons above, BCBS of Western New York and/or its affiliates, is required to provide coverage for the Optune treatment, including if applicable and necessary an exception to out of network provider.

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

DEC 16 2016

Dated: _____



Michael J. Cianci, Jr.
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Irvine, California

Appeal of:	REDACTED	OMHA Appeal No.: 1-7728219480
Beneficiary:	REDACTED	Medicare: Part B
Medicare No.:	REDACTED	Before: William J. Cowan U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is entered in the appeal of Appellant/Beneficiary REDACTED (the "Appellant/Beneficiary").

Procedural History

The Appellant/Beneficiary seeks Medicare Part B coverage and payment for an E0766 Optune Tumor Treatment Field Therapy electrical stimulation device ("Optune") with three dates of service: July 7, 2017, August 7, 2013, and September 6, 2017. Medicare Contractor CGS Administrators (the "Medicare Contractor"), denied the Appellant/Beneficiary's claim initially and on redetermination, and reconsideration was requested. (Exh. 1.)

C2C Innovative Solutions, the Qualified Independent Contractor (the "QIC"), issued an unfavorable reconsideration. The QIC found the provider, Novocure, Inc., responsible for the denied charges. On July 26, 2018, the Appellant/Beneficiary requested a hearing before an Administrative Law Judge. (Exh. 3 at 1.)

A telephone hearing was held on December 18, 2018. Appearing on behalf of the Appellant/Beneficiary were his counsel, Debra Parrish, Esq., and Julie Miles, R.N., a Clinical Appeals Specialist with Novocure, Inc., the provider. No other parties appeared. All Exhibits have been admitted into evidence without objection. (Hearing CD.)

Issue

The issue to be determined by the Administrative Law Judge ("ALJ") is:

Can Medicare reimbursement be made for the Optune device provided to the Appellant/Beneficiary for the dates of service of July 7, 2017, August 7, 2013, and September 6, 2017?

Findings of Fact

The evidence of record establishes the following facts by a preponderance of the evidence:

The Appellant/Beneficiary was a 67-year-old male diagnosed with a WHO Grade IV glioblastoma. (Exh. 2, pgs. 28, 36.) In September 2016 he underwent a near total resection of the tumor. (*Id.*) He subsequently underwent chemotherapy and radiotherapy for approximately six weeks in October and November 2017, which he tolerated well. (Exh. 2, pg. 28.) On December 8, 2018, a follow-up visit was conducted with Dr. REDACTED M.D., which included discussion of continuing treatment options including Optune treatment. (Exh. 2, pg. 30.) The Treatment Plan from that visit states: "Optune for consideration and order temozolomide. Follow up in January to begin treatment." (*Id.*)

An August 15, 2017 letter from the Appellant/Beneficiary states he began using the Optune device on January 6, 2017, and had no subsequent progression of the glioblastoma. (Exh. 1, pg. 8.)

The record includes an Optune Prescription Form signed by Dr. REDACTED and dated June 8, 2017, prescribing Optune for a 6 month period. (Exh. 2, pg. 9.) TED

The record includes an August 7, 2018 letter from CGS, the Durable Medical Equipment Medicare Administrative Contractor ("CGS"), to Novocure, regarding requested amendments to LCD 34823 to allow coverage for recurrent and newly diagnosed glioblastomas. (Exh. 4, pgs. 7-9.) The CGS letter acknowledges that coverage of newly diagnosed glioblastoma is not addressed by the LCD. (*Id.*) The letter states that based on peer-reviewed literature and NCCN information submitted by Novocure, a request for revision of the LCD to provide for coverage of the Optune device to treat newly diagnosed glioblastomas was a "valid request" on which CGS would render a final decision. The August 7, 2018 letter also found that Novocure's request for revision of the LCD to provide for coverage of the Optune device to treat recurrent tumors was not a valid request, as no new evidence or literature was provided to support it. (*Id.*)

The record includes a January 8, 2018 letter from Dr. REDACTED M.D., requesting coverage for Optune for the Appellant/Beneficiary, on the grounds that Optune is the only promising treatment option at the present time. (Exh. 1, pgs. 31-33.) Dr. REDACTED letter also notes that Optune is FDA approved as well as a National Comprehensive Cancer Network (NCCN) Category 2A recommended treatment following brain radiation with temozolomide. (*Id.*)

Legal Framework

I. ALJ Review Authority

A. Jurisdiction and Scope of Review

Section 1869(b)(1)(A) of the Act entitles an individual or organization dissatisfied with the reconsideration of an initial determination to a hearing before the Secretary of the United States Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner.

In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges within OMHA issue the final decisions of the Secretary within his scope of authority under the Act. *Id.*

The issues before an ALJ "include all of the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in a party's favor." 42 C.F.R. § 405.1032. "However, if evidence presented before the hearing causes the [ALJ] to question a favorable portion of the determination," the Judge may consider the favorable portion as an issue at the hearing after notifying the parties that he or she will do so prior to the hearing. *Id.* Further, providers and suppliers, and beneficiaries represented by providers and suppliers, must present all evidence at the reconsideration level unless there is good cause for not submitting it at or before that level. 42 C.F.R. § 405.1028.

B. Standard of Review

The Office of Medicare Hearings and Appeals ALJs conduct a "de novo" review and issue a decision based on the hearing record. 42 C.F.R. § 405.1000(d). In fulfilling this role, an ALJ qualified and appointed pursuant to the Administrative Procedure Act acts as an independent finder of fact in conducting a hearing pursuant to section 1869 of the Act. This requires a new consideration of the facts and law.

II. Principles of Law

A. Statutes and Regulations

Title XVIII of the Social Security Act ("the Act"), as amended, establishes a federally subsidized health insurance program ("Medicare") to be administered by the Department of Health and Human Services. Eligibility for Medicare benefits is determined under Title XVIII of the Act, 42 U.S.C. § 1801 et seq., and federal regulations set forth in Title 42 of the Code of Federal Regulations (C.F.R.).

Medicare Part A entitles a beneficiary to reimbursement for a variety of costs associated with hospital, related post-hospital, home health services, and hospice care for individuals eligible for Medicare. Section 1812(a)(1). Medicare Part B establishes a voluntary program of supplemental medical insurance covering physicians' charges and other medical services and supplies. (*See* Sections 1831, 1832, and 1861(s); 42 C.F.R. § 410(40)(a)(2)).

Section 1833(e) of the Act specifies that claims for payment must be supported by sufficient information and documentation to establish Medicare coverage and payment criteria have been met. The provider, supplier, or beneficiary, as appropriate, must furnish to the intermediary or carrier sufficient information to determine whether payment is due and the amount of payment. *See also* 42 C.F.R. § 424.5(a)(6).

Section 1862(a)(1)(A) of the Act provides that no payment may be made under Medicare Part A or Part B for any expenses incurred for items or services that are “not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *See also* 42 U.S.C. § 1395y(a)(1)(A), 42 C.F.R. § 411.15(k)(1)).

Section 1879 of the Act provides that when Medicare coverage and payment is excluded pursuant to Section 1862(a)(1) of the Act, payment may nevertheless be made for items or services, if neither the beneficiary nor the provider or supplier knew, and could not reasonably be expected to have known, that the items or services would not be covered or payable by Medicare. *See also* 42 C.F.R. § 411.406.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a national coverage decision (“NCD”), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. Section 1871(a)(2); 42 C.F.R. §405.860. CMS and its contractors issue guidance in the form of manuals and local medical review policies (LMRPs) or Local Coverage Determinations (LCDs). An ALJ is not bound by Carrier-issued LMRPs/LCDs or CMS policy manuals, but must give substantial deference to them. 42 C.F.R. §405.1062.

Local Coverage Determination (“LCD”) L34823 for Tumor Treatment Field Therapy (TTFT) states that “TTFT (E0766) will be denied as not reasonable and necessary.”

Analysis

The instant appeal is from a party dissatisfied with the decision of the QIC to affirm the initial determination and redetermination. The request for hearing was timely filed and there is a sufficient amount in controversy. The appeal is therefore properly before me, as the Administrative Law Judge designated to hear this case.

At issue is coverage for an E0766 Optune Tumor Treatment Field Therapy electrical stimulation device prescribed to treat the Appellant/Beneficiary’s glioblastoma.

The QIC’s reconsideration states that coverage denial is based on LCD L34823, which provides that “TTFT (E0766) will be denied as not reasonable and necessary.” (Exh. 1 at 4.) Additionally, the QIC states that there is insufficient information to quantify the effects of the device for this Appellant/Beneficiary. Thus, the QIC determined that the LCD requirements have not been met and the Optune device is not covered. (Exh. 1, pgs. 1-5.)

At the ALJ hearing, the Appellant/Beneficiary’s counsel, Debra Parrish, Esq., argued that the LCD has no quantification requirement. Furthermore, she argued, the Appellant/Beneficiary’s life expectancy with a diagnosis of glioblastoma was approximately ten months, and the fact he has survived to December 2018, or roughly 32 months after diagnosis, suffices to quantify the positive effects of the device. Additionally, Julie Miles, R.N., testified that MRI evidence showed that the Appellant/Beneficiary’s tumor had not progressed since receiving Optune treatments, and that the

average life expectancy after diagnosis with a glioblastoma was ten months without treatment. (*Hearing CD.*)

Prior to hearing Ms. Parish also submitted a written position statement which argues that the LCD does not address "newly diagnosed glioblastoma" and is therefore inapplicable and not entitled to deference in the present situation. The position statement also argues that the LCD is currently the subject of a reconsideration request and subject to revision. (*See* Exh. 4, pgs. 2-5.)

Upon review, the LCD contains no discussion of the reasons why the Optune (E0766) device will be denied as "not reasonable and necessary," much less any discussion of possible circumstances under which its use may be considered necessary. This is in contrast to peer-reviewed literature presented by the Appellant/Beneficiary which indicates that use of the Optune device is considered reasonable and necessary in the oncology community, especially for newly diagnosed glioblastoma. (*See generally*, Exh. 2, pgs. 107-370).

Through his counsel, the Appellant/Beneficiary argues that the Optune device is to be employed here to treat "newly diagnosed" Glioblastoma. The Appellant/Beneficiary argues that the Optune is FDA and National Comprehensive Cancer Network approved for treatment of newly diagnosed Glioblastoma, and is widely recognized, after numerous peer-reviewed clinical trials and studies, as a recommended treatment for recurrent and newly diagnosed Glioblastomas after standard treatments (radiation, chemotherapy) have been completed. The Appellant/Beneficiary argues that the studies show that the device prolongs survival, and many patients are doing well under this treatment regime.

In this case, the Appellant/Beneficiary has been using the device since January 6, 2017, after completion of six weeks of radiation and concurrent chemotherapy for newly diagnosed glioblastoma. Testimony was provided that normal life expectancy for this condition is 10 months. However, this patient has survived well beyond the usual 10 months and continues to exhibit no progression of the disease with this treatment. The Appellant/Beneficiary suggests that this is ample proof of effectiveness for the device. The file contains a physician letter recommending Optune for this beneficiary and requesting coverage. (Exh. 1, pgs. 31-33.) The LCD contains language indicating that coverage of Optune for recurrent glioblastoma mutiforme (GBM) is not reasonable and necessary, but does not address newly diagnosed glioblastoma. The difference is that "recurrent" indicates that the cancer tumor had recurred after standard treatments, and "newly discovered" is for tumors that have been treated with chemotherapy and radiation but have not recurred. Here, we are dealing with newly diagnosed Glioblastoma. The decision to deny is based on the general thrust of the LCD. The Optune makers have written to CMS to request amendments to the LCD to allow coverage for the newly diagnosed GBMs. (They also asked for coverage for recurrent, but that was denied.) Counsel for the Appellant/Beneficiary stated at the hearing that the plan now is for the development of a new LCD for newly discovered glioblastomas, and not to revise the existing LCD. This would mean that there is no applicable LCD that bars coverage for this device in the context of newly diagnosed glioblastomas. For all of these reasons, the record supports a favorable decision on medical necessity grounds. (I will depart from the LCD to the extent that it may be interpreted to deny coverage for the Optune device for newly diagnosed Glioblastomas). There is ample support for medical necessity here, and ample evidence of its effectiveness generally and for this Appellant/Beneficiary in particular.

Conclusions of Law

The E0766 Optune Tumor Treatment Field Therapy electrical stimulation device prescribed to the Appellant/Beneficiary is reasonable and medically necessary in accordance with Medicare law and regulations.

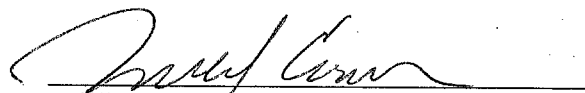
Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated:

JAN 17 2019


William J. Cowan
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Irvine, California

Appeal of: [REDACTED]	OMHA Appeal No.: 1-7916242322
Enrollee: [REDACTED]	Medicare: Part C
Medicare No.: *****9348A	Before: William J. Cowan U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented in the record, an **FULLY FAVORABLE** decision is entered in the appeal of Appellant/Enrollee [REDACTED] (the "Appellant/Enrollee").

Procedural History

The Appellant/Enrollee is an enrollee of Kaiser Permanente Senior Advantage (HMO), a Medicare PART C health plan (hereinafter "the Plan"). The Appellant/Enrollee sought pre-approval for coverage of an Optune Tumor Treatment Field Therapy ("Optune TTFT") device which was prescribed on June 27, 2018 to treat the Appellant/Enrollee's glioblastoma. The Plan denied the Appellant/Enrollee's coverage request initially and on redetermination. (Exh. 1, pgs. 19, 25.)

The Appellant/Enrollee appealed the Plan's denial to MAXIMUS Federal Services, the Part C Qualified Independent Contractor (the "QIC"). The QIC issued a reconsideration decision denying the Appellant/Enrollee's appeal. (Exh. 1, pgs. 1-5.) An appeal was filed on behalf of the Appellant/Enrollee by Novocure ("Novocure"), the maker of the Optune TTFT device, requesting a decision from an Administrative Law Judge. (Exh. 3.)

A telephone hearing was held on November 8, 2018. The Appellant/Enrollee appeared and testified on his own behalf. Appearing on behalf of Novocure were Julie Miles, R.N, its Clinical Appeals Specialist, and Dan McCoy, its Manager of Case Management. Also appearing were Piia Thomas, M.D., the Appellant/Enrollee's treating physician, and Nisha Hazari, P.A., the treating physician's assistant. No other parties appeared. All exhibits were admitted into evidence without objection. (Hearing CD.)

Additional medical records were submitted by the Appellant with the Request for Hearing and are included in the administrative record as part of Exhibit 5. Good cause exists for ALJ level

submission of new evidence under 42 C.F.R. §405.1018 because the evidence is material to an issue addressed in the QIC's reconsideration and that issue was not identified as a material issue prior to the QIC's reconsideration. All Exhibits have been admitted into evidence.

Issue

The issue to be determined by the Administrative Law Judge ("ALJ") is:

Whether the Plan must pre-approve and cover the Optune TTFT device prescribed to the Appellant/Enrollee?

Findings of Fact

The evidence of record establishes the following facts by a preponderance of the evidence:

The Appellant/Enrollee is a 65 year-old male with a high grade brain tumor. (Exh. 2, pg. 1.) He initially reported to the ED on March 23, 2018 with episodes of right sided tingling and aphasia. (*Id.*) On March 26, 2018 a biopsy was performed which confirmed a Grade III Anaplastic Astrocytoma. (Exh. 2, pg. 5.) The Appellant/Enrollee subsequently underwent chemoradiation which he tolerated well. (*Id.*) On June 26, 2018, a follow-up visit was conducted with Dr. Piia Thomas, M.D., which included review of an MRI and discussion of continuing treatment options including Optune TTFT. (*Id.*) The Progress Notes/Assessment from that visit note that Optune data –

[S]hows a statistically significant gain in OS 20 months vs 15 months) for patients with newly diagnosed GBM [glioblastoma multiforme] who use Optune. 2 year survival also improves from 26% to 43%, and 5 year survival improves from 3% to 13%.

On June 27, 2018 a prescription for Optum TTFT was completed and signed by Nisha Hazari, P.A., based on a diagnosis of malignant glioma. (Exh. 1, pg. 32.)

The record includes a letter signed by Dr. Thomas and dated September 4, 2018, which states, in relevant part:

To whom it may concern:

[REDACTED] has been under our care in the Neuro-Oncology clinic since March 2018. He underwent biopsy of a left parietal tumor on 03/26/2018 and was diagnosed with at least grade III Anaplastic Astrocytoma per the pathology report. However, further testing confirmed that the tumor did not harbor the IDH1 mutation, has EGFR amplification and is positive for monosomy 10 mutation all supporting that it is in fact an under sampled Glioblastoma (WHO grade IV). His tumor was also unmethylated suggesting less responsiveness to standard treatment.

As such, I believe he would benefit from Optune and would appreciate your consideration of him for the patient assistance program.

(Exh. 5.)

The record includes an August 7, 2018 letter from CGS, the Durable Medical Equipment Medicare Administrative Contractor (“CGS”), to Novocure, regarding requested amendments to LCD 34823 to allow coverage for recurrent and newly diagnosed glioblastomas. (Exh. 5, pgs. 9-11.) The CGS letter acknowledges that coverage of newly diagnosed glioblastoma is not addressed by the LCD. (*Id.*) The letter states that based on peer-reviewed literature and NCCN information submitted by Novocure, a request for revision of the LCD to provide for coverage of the Optune device to treat newly diagnosed glioblastoma’s was a “valid request” on which CGS would render a final decision. The August 7, 2018 letter also found that Novocure’s request for revision of the LCD to provide for coverage of the Optune device to treat recurrent tumors was not a valid request, as no new evidence or literature was provided to support it. (*Id.*)

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act (Act) § 1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges (“ALJs”) within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

A hearing before an ALJ is only available if the remaining amount in controversy is \$160 or more. *See* 42 C.F.R. § 405.1006(b)(1). The request for hearing is timely if filed within sixty days after receipt of the notice of the Qualified Independent Contractor’s (QIC’s) reconsideration. *See* 42 C.F.R. § 405.1002(a)(1).

B. Scope of Review

Under the Centers for Medicare and Medicaid Services’ (CMS) implementation policy for the Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 (BIPA), Pub. Law 106-554, app. F, 114 Stat. 2763, 2763A-463, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), Pub. Law 108-173, 117 Stat. 2066, all initial determinations by CMS-contracted carriers prior to January 1, 2006, are governed by the ALJ hearing procedures set forth at 20 C.F.R. §§ 404.929 through 404.961 and 42 C.F.R. § 405.855. *See* 70 Fed. Reg. 11420, 11424-26 (Mar. 8, 2005).

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable determination, he or she will notify the Appellant and will consider it an issue at the hearing. 20 C.F.R. § 404.946(a).

C. Standard of Review

The ALJs at OMHA conduct a "de novo" review and issue decisions based on the hearing record. 42 C.F.R. § 405.1000(d). In fulfilling this role, an ALJ qualified and appointed pursuant to the Administrative Procedure Act acts as an independent finder of fact in conducting a hearing pursuant to Section 1869 of the Social Security Act. This requires a new consideration of the facts and law.

II. Principles of Law

A. Statutes and Regulations

Title XVIII of the Social Security Act ("the Act"), as amended (42 U.S.C. §1395 *et seq.*), establishes a federally subsidized health insurance program ("Medicare") to be administered by the Department of Health and Human Services (DHHS). Eligibility for Medicare benefits is determined under Title XVIII of the Social Security Act, 42 U.S.C. §1801 *et seq.*, and federal regulations set forth in Title 42 of the Code of Federal Regulations.

Pursuant to Section 1852 of the Act, the Medicare Advantage (MA) (formerly known as Medicare+Choice) programs under Medicare Part C must provide their members with the basic benefits available under parts A and B. *See also* 42 C.F.R. §422.101. An MAO may also offer certain services that are not included in the basic benefits. 42 C.F.R. §422.102.

Medicare Part A entitles a beneficiary to reimbursement for a variety of costs associated with hospital, related post-hospital, home health services, and hospice care for individuals eligible for Medicare. Section 1812(a)(1). Medicare Part B establishes a voluntary program of supplemental medical insurance covering physicians' charges and other medical services and supplies. (*See* Sections 1831, 1832, and 1861(s); 42 C.F.R. § 410(40)(a)(2)).

Section 1833(e) of the Act specifies that claims for payment must be supported by sufficient information and documentation to establish Medicare coverage and payment criteria have been met. The provider, supplier, or beneficiary, as appropriate, must furnish to the intermediary or carrier sufficient information to determine whether payment is due and the amount of payment. *See also* 42 C.F.R. § 424.5(a)(6).

Section 1862(a)(1)(A) of the Act provides that no payment may be made under Medicare Part A or Part B for any expenses incurred for items or services that are "not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." *See also* 42 U.S.C. § 1395y(a)(1)(A), 42 C.F.R. § 411.15(k)(1)).

Medicare Advantage Organization (MAO) programs (also known as Medicare Part C) provide their members with those items and services for which benefits are available under Medicare Parts

A and B. 42 U.S.C. §1395w-22; 42 C.F.R. 422.112. An MAO is a public or private entity organized and licensed by a State as a risk-bearing entity and certified by the Center of Medicare and Medicaid Services (CMS) as meeting the Medicare Advantage contract requirements. 42 C.F.R. § 422.2. An individual is eligible to elect Medicare Part C if he or she meets the requirements set forth in 42 C.F.R. § 422.50.

The obligations of an MAO to its enrollees are set forth in Section 1852 of the Social Security Act and the implementing regulations in 42 C.F.R. Part 422. An MAO must provide coverage of all services that are covered by Part A and Part B of Medicare and that are available to enrollees residing in the plan's service area. 42 C.F.R. § 422.101. An MAO may also offer additional coverage (supplemental benefits) beyond what Medicare offers. 42 C.F.R. § 422.102. An MAO must disclose the benefits offered under a plan, including applicable conditions and limitations, premiums and cost sharing (such as copayments, deductibles, and coinsurance), and any other conditions associated with receipt or use of benefits. 42 C.F.R. § 422.111. An MAO may specify the network of providers from whom enrollees may obtain services if the MAO ensures that all covered services are available and accessible under the plan. 42 C.F.R. § 422.112.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a national coverage decision ("NCD"), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. Section 1871(a)(2); 42 C.F.R. §405.860. CMS and its contractors issue guidance in the form of manuals and local medical review policies (LMRPs) or Local Coverage Determinations (LCDs). An ALJ is not bound by Carrier-issued LMRPs/LCDs or CMS policy manuals, but must give substantial deference to them. 42 C.F.R. §405.1062.

Local Coverage Determination ("LCD") L34823 for Tumor Treatment Field Therapy (TTFT) states that "TTFT (E0766) will be denied as not reasonable and necessary."

Analysis

The instant appeal is from a party dissatisfied with the decision of the QIC to affirm the Plan's initial determination and redetermination. The request for hearing was timely filed and there is a sufficient amount in controversy. The appeal is therefore properly before me, as the Administrative Law Judge designated to hear this case.

At issue are pre-approval and coverage for an Optune TTFT – an electrical stimulation device used for cancer treatment -- prescribed on June 27, 2018 to treat the Appellant/Enrollee's glioblastoma.

The QIC's reconsideration states that denial was based on LCD L34823, which provides that "TTFT (E0766) will be denied as not reasonable and necessary." (Exh 1 at 4.) Thus, the QIC determined that the Plan does not have to pre-approve coverage for the Optune TTFT device.

At the ALJ hearing, Novocure (the maker of Optune) representatives Julie Miles, R.N, and Dan McCoy, argued on behalf of the Appellant that the Optune TTFT device is now FDA approved for treatment of "newly diagnosed" glioblastoma – newly diagnosed meaning a non-recurrent

glioblastoma cancer tumor which has undergone standard treatment, as opposed to a recurrent tumor. Additionally, it was argued the Optune TTFT is a National Comprehensive Cancer Network (“NCCN”) Category 1 treatment for glioblastoma,¹ and is widely recognized, after numerous peer-reviewed clinical trials and studies, as a recommended treatment for recurrent and newly diagnosed glioblastoma after standard treatments (radiation, chemotherapy) have been completed. It was also argued that the studies show that the Optune TTFT device prolongs survival, and many cancer patients are doing well under this treatment regime. Additionally, it was asserted that many appeals akin to this one have been found favorably for the appellant with respect to coverage of the Optune TTFT device.

The LCD contains no discussion of the reasons why “TTFT (E0766) will be denied as not reasonable and necessary,” much less any discussion of the types of cancers the device is used to treat or possible circumstances under which its use may be considered necessary. This is in contrast to the literature presented on behalf of the Appellant, which is strongly indicative that use of the Optune device is considered a reasonable and necessary treatment in the oncology community and is covered by insurers in many cases, especially in the case of newly diagnosed glioblastomas subsequent to standard treatments (radiation, chemotherapy). For example, Aetna insurance Publication Number 0827 (March 19, 2013) regarding Electric Tumor Treatment Fields states in relevant part:²

Aetna considers devices to generate electric tumor treatment fields (ETTF) medically necessary as monotherapy for persons with histologically confirmed glioblastoma (World Health Organization grade IV astrocytoma), after histologically or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy.

Aetna considers combination of devices to generate ETTF and temozolomide medically necessary as adjunctive treatment of newly-diagnosed histologically confirmed supratentorial glioblastoma following standard treatments that include surgery, chemotherapy, and radiation therapy.

....

On October 5, 2015, the FDA approved an expanded indication for the Optune device (using alternating electrical fields called “tumor treatment fields” [TTFields]) to treat patients with newly-diagnosed GBM. It is administered along with temozolomide (TMZ) following standard treatments that include surgery, chemotherapy, and radiation therapy. In the clinical study used to support the expanded indication, patients treated with the device and TMZ lived on average 3 months longer than those treated with the drug alone. Optune was initially

¹ Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. (www.nccn.org)

² Clinical policy bulletin: electric tumor treatment fields. Number: 0827. [internet]. Hartford (CT): Aetna, Inc.; 2013 Mar 19 [accessed 2013 Sept 16]. Available: http://www.aetna.com/cpb/medical/data/800_899/0827.html.

approved in 2011 to treat patients with GBM that recurred or progressed after chemotherapy. With this expanded indication, Optune can be used as part of a standard treatment for GBM before the disease progresses. For newly diagnosed GBM, Optune is not intended to be used as a substitute for standard treatments, but rather as an adjunct therapy. The device is portable and can be powered with batteries or plugged into an electrical outlet. Patients can use the device at home or work, allowing them to continue their normal daily activities.

The FDA based its approval of the expanded indication of the Optune device on results from a clinical trial involving 695 patients newly diagnosed with GBM that compared those who used Optune with TMZ to those receiving TMZ alone. Patients who used the device along with TMZ lived, on average, about 7 months with no disease progression compared to 4 months for those who had the drug alone. The Optune plus TMZ group survived for an average of 19.4 months after diagnosis compared to 16.6 months for those who were treated with only TMZ. The most common side effect experienced with Optune was skin irritation. Clinical trial participants also experienced a slightly higher incidence of neurological side effects, including convulsions and headaches, compared to subjects receiving TMZ alone. Patients should not use the Optune system if they have an active implanted medical device or a skull defect, have an underlying skin condition involving the scalp or have a known sensitivity to conductive hydrogels, such as those used on electrocardiogram stickers.

(*Id.*) Such sources as the one quoted above indicate that there are certain instances, such as with newly diagnosed glioblastoma, where Optune therapy may be considered reasonable and medically necessary in addition to standard treatments. Novocure representative Dan McCoy stated that Novocure wrote to the DME Medicare Administrative Contractor CGS (“CGS”), to request amendments to the LCD to allow coverage for newly diagnosed glioblastomas. By letter dated August 7, 2018, CGS acknowledged that coverage of newly diagnosed glioblastoma is not addressed by the LCD. (Exh. 5, pgs. 9-11.) CGS also confirmed that based on peer-reviewed literature and NCCN information submitted by Novocure, the request for revision of the LCD to provide for coverage of the Optune device to treat newly diagnosed glioblastoma’s was a “valid request” on which CGS would render a final decision. (*Id.*) That request is pending. (The August 7, 2018 letter also found that Novocure’s request for revision of the LCD to provide for coverage of the Optune device to treat *recurrent* tumors was not a valid request, as no new evidence or literature was provided to support it.)

IN addition to the above, it should also be noted that the Appellant/Enrollee’s treating physician, Dr. Thomas submitted an opinion letter recommending treatment with the Optune device, and testified persuasively at the hearing that the device is medically necessary for him.

In the present case, we are dealing with newly diagnosed Glioblastoma. There is ample evidence in the record to support a favorable decision in this case, and therefore I will depart from the LCD to the extent that it may be interpreted to deny coverage for TTFT for newly diagnosed glioblastomas.³ The literature and information provided strongly support a finding of medical necessity here, and the treating physician and physician’s assistant are on the record in support of

³ AS noted above, CGS acknowledged that coverage of newly diagnosed glioblastoma is not addressed by the LCD.

coverage. The Plan itself did not appear and no evidence was submitted to indicate the Optune TTFT device is not medically necessary under the facts of this case.

Based on the foregoing, I find that the record establishes that the Optune TTFT device (E0766) prescribed to the Appellant/Enrollee is reasonable and medically necessary in accordance with Medicare law and regulations.

Conclusions of Law

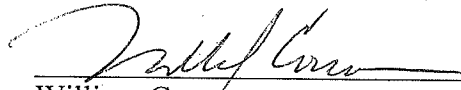
The Optune TTFT device (E0766) prescribed to the Appellant/Enrollee is reasonable and medically necessary in accordance with Medicare law and regulations.

Order

The Plan is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated: **NOV 27 2018**



William Cowan
U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri**

Appeal of: **Novocure Inc.**

ALJ Appeal No.: **1-2557792267**

Beneficiary: **The Est. of**

Medicare Part B

HICN: *******7777A**

Before: **Roger Davis**
U.S. Administrative Law Judge

DECISION

This Judge decides this appeal **fully favorable** to Novocure Inc. (the “Appellant”) after holding a telephonic hearing.

Findings of Fact

The Appellant seeks coverage of NovoTTF-100A HCPCS code E1399 billed on April 21, 2013; May 21, 2013; June 21, 2013; and July 21, 2013 for treatment of progressive glioblastoma multiform (GBM)¹. This device is relatively new to cancer treatment. This non-invasive system is used in the beneficiary’s home, and delivers tumor treating fields therapy (TTF) to the brain to disrupt rapid cell division exhibited by recurrent GBM tumors. The system is comprised of a durable electrical field generator and disposable insulated transducer arrays (worn affixed to the scalp) for use with the portable generator. The system also includes lithium ion batteries, battery rack, battery charger, power supply, connection cables, and a carrying case. (Ex. 6, pp. 10-22.) The device is indicated for treatment of adult patients with histologically-confirmed glioblastoma multiforme, following histologically or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 6, pp. 5-7.)

¹ On January 1, 2014, CMS created a new code, E0766, to group all billing, including all components/supplies and monthly rental fees, for NovoTTF-100A. Prior to this new code, the Appellant used multiple miscellaneous codes to bill the items, including: A9999, A9900, E1399, and A4555. This Judge takes note of the different codes used to bill the device, but does not purport to dictate how or under which code payment should be affected and/or authorized. The legal analysis will address whether coverage is supported by the documentation submitted.

This device is manufactured by NovoCure, Ltd., and was approved by the Federal and Drug Administration (FDA) in April of 2011. (Ex. 6, pp. 5-7.) The device was approved after the pre-market approval pathway (PMA). This is the most rigorous medical device approval pathway, and is analogous to the FDA new drug pathway. The FDA approved the device on the basis of a multi-center randomized controlled pivotal (phase III) clinical trial. This was then followed by a positive vote from the FDA's independent Medical Device Advisory Committee's Neurological Devices Panel. (*Id.*) The device falls within the DME benefit category according to a July 26, 2013 letter from CMS. (Ex. 6, pg. 2.) The device is also included in the National Comprehensive Cancer Network Guidelines ("NCCN Guidelines") for recurrent glioblastoma, which is the standard of care for the diagnosis. The NCCN Guidelines are not binding in making Medicare coverage decisions. (Ex. 6, pg. 3.)

The beneficiary was a 65-year-old female diagnosed with recurrent glioblastoma multiforme progressive. (Ex. 1, pp. 24-27, 59-61; Ex. 3, pp. 2-5, 10; Hearing CD.) Glioblastomas (GBM) are tumors that arise from astrocytes—the star-shaped cells that make up the “glue-like,” or supportive tissue of the brain. These tumors are usually highly malignant because the cells reproduce quickly and they are supported by a large network of blood vessels. (See <http://www.abta.org/brain-tumor-information/types-of-tumors/glioblastoma.html>.) Recurrent glioblastoma multiforme progressive is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. There are few, if any, available options that would benefit the patient in this clinical scenario. Patients with recurrent GBM have a one-year survival rate of approximately 10% and a median overall survival time of three to five months when not treated with an effective (active) therapy. (Ex. 6, pp. 10-22.)

The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by concomitant chemotherapy and radiation using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

The records indicate that _____ was a 65-year-old female diagnosed with GBM grade IV that was supratentorial in location. (Ex. 1, pp. 24-27, 59-61; Ex. 3, pp. 2-5, 10; Hearing CD.) The tumor was recurrent. (*Id.*) Her treating physician recommended beginning TTF treatment on September 21, 2012, as the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (*Id.*)

The beneficiary's medical records show that _____ initially presented to the hospital with mental status changes and complaints of headaches, achiness, and chest discomfort. (Ex. 1, pp. 24-27, 59-61; Ex. 3, pp. 2-5, 10; Hearing CD.) Additionally, she had difficulty expressing her thoughts and understanding what others communicated to her. (*Id.*) A CT scan revealed a left parietal lesion with a subacute ischemic stroke. (*Id.*) She had a biopsy on May 23, 2011 which indicated GBM grade IV. (*Id.*) After gross total resection on July 7, 2011, she received

radiation therapy with concurrent Temodar from August 2, 2011 to September 20, 2011. (*Id.*) Shortly after initiating standard Temodar in November 2011, she suffered from a Steven-Johnson Syndrome rash with severe pancytopenia, therefore Temodar was not a viable option for her. (*Id.*) In January of 2012, attempted an immune-boosting alternative therapy called “Amiocare-A10 forte” but did not tolerate this well. (*Id.*) Her MRIs were stable. (*Id.*) Her treating physician recommended that she begin TTFields therapy on September 21, 2012. (*Id.*)

Procedural History

The Medicare Administrative Contractor denied coverage for the Part A medical equipment the Appellant billed. Then the Qualified Independent Contractor issued an unfavorable decision on the Appellant’s appeal. Finally, the Appellant filed a request for a hearing before an Administrative Law Judge (“ALJ” or “Judge”) with the Office of Medicare Hearings and Appeals (“OMHA”).

This Judge conducted a hearing with representatives of the Appellant on February 15, 2018. All evidence was admitted, and accordingly, the administrative record is now closed.

Legal Framework

I. ALJ Review Authority

Health Plan enrollees who are dissatisfied with their Health Plan because they did not receive healthcare to which they believe they were entitled to, or because they contest the cost of a service they received, are entitled to an appeal process. Social Security Act § 1852(g), 42 U.S.C. § 1395w-22(g), 42 C.F.R. §§ 422.560, 422.562. The appeal process includes, if necessary, a hearing before an ALJ. 42 C.F.R. § 422.562(b)(4). An ALJ within the Office of Medicare Hearing and Appeals shall perform a *de novo* review of the case provided that there is a sufficient amount in controversy and that the appellant files the appeal in a timely fashion. 42 U.S.C. § 1395ff(b)(1)(A); *see also* 42 C.F.R. §§ 422.600, 405.1000 and 405.1002. *See generally* 70 Fed. Reg. 36386, 36387 (June 23, 2005) (delegation of Secretary’s power specifically to OMHA to conduct reviews).

II. Principles of Law

I. ALJ Review Authority

A. Jurisdiction

Individuals or organizations dissatisfied with the reconsideration of an initial determination are entitled to hearings before the Secretary of the Department of Health and Human Services. There must be a sufficient amount in controversy at the time of the request for hearing, and the appellant must timely submit the request for hearing. (42 C.F.R. § 405.1014; Social Security Act (“the Act”) § 1869(b)(1)(A)). The Secretary delegates OMHA to administer the nationwide hearings and appeals system, and the ALJs within OMHA issue the final decisions of the

Secretary, unless later reviewed by the Medicare Appeals Council. (*See* 70 Fed. Reg. 36386, 36387 (June 23, 2005)).

The request for hearing is timely if the Appellant files within sixty days after they receive the QIC Reconsideration determination. (*See* 42 C.F.R. §405.1002(a)(1)).

For requests filed in calendar year 2013, the required minimum amount remaining in controversy for an ALJ hearing is \$140.00 (following application of any co-insurance or deductible). (42 C.F.R. § 405.1006(b)(1)).

B. Scope of Review

The issues before the ALJ include any issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. (42 C.F.R. § 405.1000; 405.1032).

C. Standard of Review

The ALJ conducts a *de novo* review and issues a decision based on the hearing record. (42 § C.F.R. § 405.1000(d)). *De novo* review requires the ALJ to evaluate the record and controlling laws and render an independent assessment without regard to prior determinations and findings on the claim. All laws and regulations pertaining to Medicare are binding on ALJs, including but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations.

The Appellant bears the burden of proving each element of a Medicare claim by a preponderance of the evidence. This is satisfied through the submission of sufficient evidence in accordance with Medicare rules. (*See* §§1814(a)(1), 1815(b), and 1833(e) of the Act; 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, 405.1030).

I. Principles of Law

A. Statutes and Regulations

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services (CMS). Section 1831 of the Act establishes the Supplemental Medical Insurance Program for the aged and disabled under Part B.

Section 1832 of the Act establishes the scope of benefits provided to beneficiaries under the Medicare Part B insurance program. Under Section 1832(a)(2)(B) of the Act, an individual is entitled to payment for medical and other health services furnished by a provider of services, or by others as arranged by the provider of services. (*See also* 42 C.F.R. §410.3). No payment shall be made to any provider under the Act unless the provider furnishes information to determine the amounts due to them for the period at issue. (*See* 42 C.F.R. § 424.5(a)(6); and Title XVIII, § 1833(e) of the Act).

Medicare will pay for services that are reasonable and medically necessary for the diagnosis or treatment of a condition, illness, or injury to the beneficiary, or to improve the functioning of a malformed body member. (42 USC § 1395d(a)(1)). The provider must provide sufficient documentation to support the claim for payment. (42 C.F.R. § 424.5 (a)(6)).

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. Although not subject to the force and effect of law, CMS and its contractors have issued policy and guidelines describing the coverage criteria for selected types of medical services and supplies.

42 CFR Section 414.202 and the Chapter 15, Section 110.1 of the Medicare Benefit Policy Manual (CMS Publ. 100-2) provides, in relevant part, that durable medical equipment (“DME”) means equipment, furnished by a supplier or home health agency that –

- 1) Can withstand repeated use;
- 2) Is primarily and customarily used to serve a medical purpose;
- 3) Generally is not useful to an individual in the absence of an illness or injury; and
- 4) Is appropriate for use in the home.

Section 1879(a)(1) of Title XVIII of the Social Security Act provides in pertinent part, that when Medicare coverage is precluded under Section 1862(a)(1)(A) of the Act, i.e. the billed services were not reasonable and necessary, payment will be made, despite the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably been expected to know that the item was not covered. This is the limitation of liability provision. In other words, if either the beneficiary or the provider knew or had reason to know the service would not be covered, they are responsible for payment.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (“LMRPs”) or local coverage determinations (“LCDs”).

On the date of service at issue, no NCD or LCDs were in effect to enumerate coverage requirements for the medical device at issue.

Medically Reasonable and Necessary Medical Services

Part B of the Medicare Act extends coverage to certain types of durable medical equipment (DME) for qualified recipients. 42 U.S.C. § 1395k(a); *id.* § 1395x(s)(6). Not all DME is guaranteed coverage under Medicare Part B, however. The Medicare statute explicitly provides that “no payment may be made under ... Part B of this subchapter for any expenses incurred for items ... [which] are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *Id.* § 1395y(a)(1)(A); *see also Almy v. Sebelius*, 679 F.3d 297, 299 (4th Cir. 2012).

Medicare coverage of DME is determined in one of three ways. First, Medicare issues a “national coverage determination” (NCD) binding throughout the Medicare system and not subject to review by administrative law judges. *Id.* § 1395ff(f)(1)(B). Second, one of the private insurance carriers with whom Medicare contracts to administer claims under Part B can issue a “local coverage determination” (LCD) “respecting whether or not a particular item or service is covered on an intermediary – or carrier-wide basis.” *Id.* § 1395ff(f)(2)(B); *see also Almy*, 679 F.3d at 299. Finally, if no NCD or LCD is in place, “contractors may make individual claim determinations,” including whether a particular DME meets the statutory requirement of being “reasonable and necessary.” 68 Fed. Reg. 63, 693.

Medicare also has developed guidance in the Medicare Program Integrity Manual (CMS Pub. 100-08) (MPIM), Ch. 13 at § 13.5.1, and the Medicare Benefit Policy Manual (CMS Pub. 100-02) (MBPM), Ch. 15 at § 110 for Medicare contractors applying the “reasonable and necessary” standard.² A device is not “reasonable and necessary” – and thus is not eligible for Medicare coverage – if it is:

- Not “safe” and “effective” – that is, if the device has not “been proven safe and effective based on authoritative evidence” or is not “generally accepted in the medical community as safe and effective for the condition for which it is used”;
- “[E]xperimental” – that is, “investigational”;
- Not “[a]ppropriate” for the individual beneficiary’s needs; or
- “[S]ubstantially more costly than a medically appropriate and realistically feasible alternative pattern of care.”

See also Almy, 679 F.3d at 299; *Int’l Rehabilitative Scis. Inc. v. Sebelius*, 688 F.3d 994, 997 (9th Cir. 2012).

The burden is on the claimant to show that the device is reasonable and necessary. *Almy*, 679 F.3d at 305.

Medicare also instructs contractors as to the type of evidence to be used in making these technical determinations. Such decisions should be based on either “published authoritative evidence” such as “definitive randomized clinical trials” or “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not

² ALJs and the Medicare Appeals Council are not bound by CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. 42 C.F.R. § 405.1062(a).

sufficient evidence of general acceptance by the medical community.” MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

Statement of the Issues

1. Whether all Medicare coverage requirements have been met warranting payment under Title XVIII of the Social Security Act?
2. Whether the limitation on liability provisions of Section 1879 are applicable?

Analysis

The crux of the issue in this appeal is whether the record establishes that the medical device at issue was medically reasonable and necessary for treatment of the beneficiary’s condition. The Qualified Independent Contractor (QIC) denied coverage for the medical equipment, reasoning that the device had not been deemed a safe and effective treatment. The QIC found the Appellant liable for the non-covered charges. (Ex. 1, pp. 1-7.)

This Judge is aware that there is an LCD, specifically *CGS Admin., Local Coverage Determination L34665: Tumor Treatment Field Therapy (LCD L34665) (Oct. 2014)*. However, the LCD was not yet in effect on the dates of service at issue, and only summarily denies coverage stating that the device was not reasonable and necessary. This Judge also has reviewed three other LCD jurisdictions in search of further information and guidance, however, they provide no additional information. This Judge speculates that the LCDs lack details because the scientific evidence of the effectiveness of this therapy has only recently developed and the LCDs have not yet caught up with recent developments.

Pursuant to 42 C.F.R. § 405.1062, ALJs are not bound by LCDs, but will give substantial deference to these policies if they are applicable to a particular case. Furthermore, if an ALJ declines to follow a policy in a particular case, the ALJ must explain the reasons why the policy was not followed. *See* 42 C.F.R. § 405.1062. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect. *See id.*

This Judge finds that the therapy in question has been proven to be safe and effective and is medically reasonable and necessary to treat this particular beneficiary’s condition. This Judge explains his rationale as follows:

TTF Therapy Has Been Proven Safe and Effective Based on Authoritative Evidence

Because there is no NCD or LCD in effect on the dates of service at issue (E1399/A9999), this Judge must decide whether TTF has been proven safe and effective based on authoritative evidence. (MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110; *see also Almy*, 679 F.3d at 299). Such decisions should be based on either “published authoritative evidence” such as “definitive randomized clinical trials” or “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

Based on the hearing testimony; medical evidence and studies submitted; NCCN Guidelines; and FDA approval of the device, this Judge finds that the device in question has been proven safe and effective based on authoritative evidence.

The record supports that recurrent glioblastoma multiforme is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. Recent clinical studies of the effect of treating GBM patients with TTF therapy with Temozolomide have shown significant improvements – approximately 50% – in survival rates. The safety and efficacy of TTF therapy is generally accepted in the medical community. After a thorough review of the clinical studies, this Judge finds the studies creditable in establishing the efficacy of TTF therapy in prolonging and improving the survival of patients diagnosed with GBM.

Finally, this Judge finds that the device is FDA approved, which is further evidence that it is “safe” and “effective.” Medicare law states that FDA clearance is *necessary*, but not *sufficient*, for Medicare coverage. (*Int’l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Specifically, FDA review seeks to determine whether a device is “safe and effective” such that it can be marketed to the general public. By contrast, Medicare coverage review seeks to determine whether the device is “reasonable and necessary” for treatment such that the device is worth the government’s money. (MBPM, ch. 15, § 110.1; *Int’l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Therefore, this Judge finds FDA approval to be further evidence of the device’s safety and effectiveness.

TTF Therapy is Medically Reasonable and Necessary to Treat this Particular Beneficiary’s Condition

This Judge finds the TTF therapy device at issue to be medically reasonable and necessary for the beneficiary because it is an appropriate treatment of the beneficiary’s condition and since there is no medically appropriate and realistically feasible alternative pattern of care for the beneficiary. (MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110).

First, this Judge takes into account the medical record and hearing testimony. The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by concomitant chemotherapy and radiation using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

The records indicate that _____ was a 65-year-old female diagnosed with GBM grade IV that was supratentorial in location. (Ex. 1, pp. 24-27, 59-61; Ex. 3, pp. 2-5, 10; Hearing CD.) The tumor was recurrent. (*Id.*) Her treating physician recommended beginning TTF treatment on September 21, 2012, as the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (*Id.*)

The beneficiary's medical records show that [redacted] initially presented to the hospital with mental status changes and complaints of headaches, achiness, and chest discomfort. (Ex. 1, pp. 24-27, 59-61; Ex. 3, pp. 2-5, 10; Hearing CD.) Additionally, she had difficulty expressing her thoughts and understanding what others communicated to her. (*Id.*) A CT scan revealed a left parietal lesion with a subacute ischemic stroke. (*Id.*) She had a biopsy on May 23, 2011 which indicated GBM grade IV. (*Id.*) After gross total resection on July 7, 2011, she received radiation therapy with concurrent Temodar from August 2, 2011 to September 20, 2011. (*Id.*) Shortly after initiating standard Temodar in November 2011, she suffered from a Steven-Johnson Syndrome rash with severe pancytopenia, therefore Temodar was not a viable option for her. (*Id.*) In January of 2012, [redacted] attempted an immune-boosting alternative therapy called "Amiocare-A10 forte" but did not tolerate this well. (*Id.*) Her MRIs were stable. (*Id.*) Her treating physician recommended that she begin TTFields therapy on September 21, 2012. (*Id.*)

This Judge also takes into account the FDA approval letter, which sets forth specific criteria for beneficiaries who would be considered candidates for TTF therapy delivered by the Appellant:

This device is indicated for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically – or radiologically – confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy³, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 6, pp. 5-7.)

This Judge finds that the beneficiary meets all the criteria set forth by the FDA and the NCCN Guidelines.

Based on the foregoing evidence, this Judge finds that the TTF therapy device at issue has been proven to be safe and effective and is medically reasonable and necessary to treat the beneficiary's condition.

Conclusions of Law

Based upon the written evidence in the record and the testimony offered at the hearing, this Judge issues a **fully favorable** determination for Novocure Inc. Medicare coverage is appropriate under Medicare Part B for the NovoTTF-100A HCPCS code E1399 billed on April 21, 2013; May 21, 2013; June 21, 2013; and July 21, 2013 for [redacted]. Coverage is supported by sufficient information as required by Sections 1862(a) and 1833(e) of the Social Security Act.

³ This Judge notes that since this FDA approval letter dated April 8, 2011, the FDA has approved the Appellant's device* in combination with temozolomide for the treatment of adult patients with newly diagnosed GBM. See http://www.abta.org/about-us/news/brain-tumor-news/fda-approves-optune-in_oct15.html

Order

The Medicare contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

APR 23 2018

Dated: _____


Roger Davis
U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri**

Appeal of: Novocure Inc.	ALJ Appeal No.: 1-2562072331
Beneficiary: The Est. of	Medicare Part B
HICN: *****2832A	Before: Roger Davis U.S. Administrative Law Judge

DECISION

This Judge decides this appeal **fully favorable** to Novocure Inc. (the “Appellant”) after holding a telephonic hearing.

Findings of Fact

The Appellant seeks coverage of NovoTTF-100A HCPCS code A9900 billed on April 23, 2013; June 5, 2013; and August 12, 2013 for treatment of progressive glioblastoma multiform (GBM)¹. This device is relatively new to cancer treatment. This non-invasive system is used in the beneficiary’s home, and delivers tumor treating fields therapy (TTF) to the brain to disrupt rapid cell division exhibited by recurrent GBM tumors. The system is comprised of a durable electrical field generator and disposable insulated transducer arrays (worn affixed to the scalp) for use with the portable generator. The system also includes lithium ion batteries, battery rack, battery charger, power supply, connection cables, and a carrying case. (Ex. 6, pp. 141-63.) The device is indicated for treatment of adult patients with histologically-confirmed glioblastoma multiforme, following histologically or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 6, pp. 130-34.)

¹ On January 1, 2014, CMS created a new code, E0766, to group all billing, including all components/supplies and monthly rental fees, for NovoTTF-100A. Prior to this new code, the Appellant used multiple miscellaneous codes to bill the items, including: A9999, A9900, E1399, and A4555. This Judge takes note of the different codes used to bill the device, but does not purport to dictate how or under which code payment should be affected and/or authorized. The legal analysis will address whether coverage is supported by the documentation submitted.

This device is manufactured by NovoCure, Ltd., and was approved by the Federal and Drug Administration (FDA) in April of 2011. (Ex. 6, pp. 130-34.) The device was approved after the pre-market approval pathway (PMA). This is the most rigorous medical device approval pathway, and is analogous to the FDA new drug pathway. The FDA approved the device on the basis of a multi-center randomized controlled pivotal (phase III) clinical trial. This was then followed by a positive vote from the FDA's independent Medical Device Advisory Committee's Neurological Devices Panel. (*Id.*) The device falls within the DME benefit category according to a July 26, 2013 letter from CMS. (Ex. 6, pg. 126.) The device is also included in the National Comprehensive Cancer Network Guidelines ("NCCN Guidelines") for recurrent glioblastoma, which is the standard of care for the diagnosis. The NCCN Guidelines are not binding in making Medicare coverage decisions. (Ex. 6, pp. 127-29.)

The beneficiary was a 57-year-old male diagnosed with recurrent glioblastoma multiforme progressive. (Ex. 1, pp. 21-24; Ex. 3, pp. 5-6, 9-11; Hearing CD.) Glioblastomas (GBM) are tumors that arise from astrocytes—the star-shaped cells that make up the “glue-like,” or supportive tissue of the brain. These tumors are usually highly malignant because the cells reproduce quickly and they are supported by a large network of blood vessels. (See <http://www.abta.org/brain-tumor-information/types-of-tumors/glioblastoma.html>). Recurrent glioblastoma multiforme progressive is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. There are few, if any, available options that would benefit the patient in this clinical scenario. Patients with recurrent GBM have a one-year survival rate of approximately 10% and a median overall survival time of three to five months when not treated with an effective (active) therapy. (Ex. 6, pp. 141-63.)

The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by concomitant chemotherapy and radiation using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

The records indicate that [redacted] was a 57 year old male diagnosed with progressive left temporal glioblastoma that was supratentorial in location. (Ex. 1, pp. 21-24; Ex. 3, pp. 5-6, 9-11; Hearing CD.) The tumor was recurrent. (*Id.*) His treating physician recommended beginning TTF treatment on December 5, 2012, as the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (*Id.*)

The beneficiary's medical records show that [redacted] initially was diagnosed with glioblastoma on February 27, 2007. (Ex. 1, pp. 21-24; Ex. 3, pp. 5-6, 9-11; Hearing CD.) He received concurrent radiation and chemotherapy with Temozolomide and Keppra after the first surgery. (*Id.*) Due to another tumor progression, he had a second surgery on September 16, 2009. (*Id.*) He then received Temodar and Thalidomide until February 2012. (*Id.*) After a third craniotomy on March 9, 2013, he had a seizure involving his right side, face, and arm. (*Id.*) He

also suffered from expressive aphasia as a result of the third surgery and mild comprehension difficulty. (*Id.*) Due to myelosuppression, his chemotherapy was put on hold. (*Id.*) Due to his recurrent glioblastoma, treating physician recommended that he begin TTFields therapy on December 5, 2012. (*Id.*)

Procedural History

The Medicare Administrative Contractor denied coverage for the Part A medical equipment the Appellant billed. Then the Qualified Independent Contractor issued an unfavorable decision on the Appellant's appeal. Finally, the Appellant filed a request for a hearing before an Administrative Law Judge ("ALJ" or "Judge") with the Office of Medicare Hearings and Appeals ("OMHA").

This Judge conducted a hearing with representatives of the Appellant on March 16, 2018. All evidence was admitted, and accordingly, the administrative record is now closed.

Legal Framework

I. ALJ Review Authority

Health Plan enrollees who are dissatisfied with their Health Plan because they did not receive healthcare to which they believe they were entitled to, or because they contest the cost of a service they received, are entitled to an appeal process. Social Security Act § 1852(g), 42 U.S.C. § 1395w-22(g), 42 C.F.R. §§ 422.560, 422.562. The appeal process includes, if necessary, a hearing before an ALJ. 42 C.F.R. § 422.562(b)(4). An ALJ within the Office of Medicare Hearing and Appeals shall perform a *de novo* review of the case provided that there is a sufficient amount in controversy and that the appellant files the appeal in a timely fashion. 42 U.S.C. § 1395ff(b)(1)(A); *see also* 42 C.F.R. §§ 422.600, 405.1000 and 405.1002. *See generally* 70 Fed. Reg. 36386, 36387 (June 23, 2005) (delegation of Secretary's power specifically to OMHA to conduct reviews).

II. Principles of Law

I. ALJ Review Authority

A. Jurisdiction

Individuals or organizations dissatisfied with the reconsideration of an initial determination are entitled to hearings before the Secretary of the Department of Health and Human Services. There must be a sufficient amount in controversy at the time of the request for hearing, and the appellant must timely submit the request for hearing. (42 C.F.R. § 405.1014; Social Security Act ("the Act") § 1869(b)(1)(A)). The Secretary delegates OMHA to administer the nationwide hearings and appeals system, and the ALJs within OMHA issue the final decisions of the Secretary, unless later reviewed by the Medicare Appeals Council. (*See* 70 Fed. Reg. 36386, 36387 (June 23, 2005)).

The request for hearing is timely if the Appellant files within sixty days after they receive the QIC Reconsideration determination. (*See* 42 C.F.R. §405.1002(a)(1)).

For requests filed in calendar year 2013, the required minimum amount remaining in controversy for an ALJ hearing is \$140.00 (following application of any co-insurance or deductible). (42 C.F.R. § 405.1006(b)(1)).

B. Scope of Review

The issues before the ALJ include any issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. (42 C.F.R. § 405.1000; 405.1032).

C. Standard of Review

The ALJ conducts a *de novo* review and issues a decision based on the hearing record. (42 § C.F.R. § 405.1000(d)). *De novo* review requires the ALJ to evaluate the record and controlling laws and render an independent assessment without regard to prior determinations and findings on the claim. All laws and regulations pertaining to Medicare are binding on ALJs, including but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations.

The Appellant bears the burden of proving each element of a Medicare claim by a preponderance of the evidence. This is satisfied through the submission of sufficient evidence in accordance with Medicare rules. (*See* §§1814(a)(1), 1815(b), and 1833(e) of the Act; 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, 405.1030).

I. Principles of Law

A. Statutes and Regulations

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services (CMS). Section 1831 of the Act establishes the Supplemental Medical Insurance Program for the aged and disabled under Part B.

Section 1832 of the Act establishes the scope of benefits provided to beneficiaries under the Medicare Part B insurance program. Under Section 1832(a)(2)(B) of the Act, an individual is entitled to payment for medical and other health services furnished by a provider of services, or by others as arranged by the provider of services. (*See also* 42 C.F.R. §410.3). No payment shall be made to any provider under the Act unless the provider furnishes information to determine the amounts due to them for the period at issue. (*See* 42 C.F.R. § 424.5(a)(6); and Title XVIII, § 1833(e) of the Act).

Medicare will pay for services that are reasonable and medically necessary for the diagnosis or treatment of a condition, illness, or injury to the beneficiary, or to improve the functioning of a

malformed body member. (42 USC § 1395d(a)(1)). The provider must provide sufficient documentation to support the claim for payment. (42 C.F.R. § 424.5 (a)(6)).

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. Although not subject to the force and effect of law, CMS and its contractors have issued policy and guidelines describing the coverage criteria for selected types of medical services and supplies.

42 CFR Section 414.202 and the Chapter 15, Section 110.1 of the Medicare Benefit Policy Manual (CMS Publ. 100-2) provides, in relevant part, that durable medical equipment (“DME”) means equipment, furnished by a supplier or home health agency that –

- 1) Can withstand repeated use;
- 2) Is primarily and customarily used to serve a medical purpose;
- 3) Generally is not useful to an individual in the absence of an illness or injury; and
- 4) Is appropriate for use in the home.

Section 1879(a)(1) of Title XVIII of the Social Security Act provides in pertinent part, that when Medicare coverage is precluded under Section 1862(a)(1)(A) of the Act, i.e. the billed services were not reasonable and necessary, payment will be made, despite the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably been expected to know that the item was not covered. This is the limitation of liability provision. In other words, if either the beneficiary or the provider knew or had reason to know the service would not be covered, they are responsible for payment.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (“LMRPs”) or local coverage determinations (“LCDs”).

On the date of service at issue, no NCD or LCDs were in effect to enumerate coverage requirements for the medical device at issue.

Medically Reasonable and Necessary Medical Services

Part B of the Medicare Act extends coverage to certain types of durable medical equipment (DME) for qualified recipients. 42 U.S.C. § 1395k(a); *id.* § 1395x(s)(6). Not all DME is guaranteed coverage under Medicare Part B, however. The Medicare statute explicitly provides

that “no payment may be made under ... Part B of this subchapter for any expenses incurred for items ... [which] are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *Id.* § 1395y(a)(1)(A); *see also Almy v. Sebelius*, 679 F.3d 297, 299 (4th Cir. 2012).

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Medicare also has developed guidance in the Medicare Program Integrity Manual (CMS Pub. 100-08) (MPIM), Ch. 13 at § 13.5.1, and the Medicare Benefit Policy Manual (CMS Pub. 100-02) (MBPM), Ch. 15 at § 110 for Medicare contractors applying the “reasonable and necessary” standard.² A device is not “reasonable and necessary” – and thus is not eligible for Medicare coverage – if it is:

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See also Almy, 679 F.3d at 299; *Int’l Rehabilitative Scis. Inc. v. Sebelius*, 688 F.3d 994, 997 (9th Cir. 2012).

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Statement of the Issues

1. Whether all Medicare coverage requirements have been met warranting payment under Title XVIII of the Social Security Act?
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The crux of the issue in this appeal is whether the record establishes that the medical device at issue was medically reasonable and necessary for treatment of the beneficiary's condition. The Qualified Independent Contractor (QIC) denied coverage for the medical equipment, reasoning that the device had not been deemed a safe and effective treatment. The QIC found the Appellant liable for the non-covered charges. (Ex. 1, pp. 1-7.)

This Judge is aware that there is an LCD, specifically *CGS Admin., Local Coverage Determination L34665: Tumor Treatment Field Therapy (LCD L34665) (Oct. 2014)*. However, the LCD was not yet in effect on the dates of service at issue, and only summarily denies coverage stating that the device was not reasonable and necessary. This Judge also has reviewed three other LCD jurisdictions in search of further information and guidance, however, they provide no additional information. This Judge speculates that the LCDs lack details because the scientific evidence of the effectiveness of this therapy has only recently developed and the LCDs have not yet caught up with recent developments.

Pursuant to 42 C.F.R. § 405.1062, ALJs are not bound by LCDs, but will give substantial deference to these policies if they are applicable to a particular case. Furthermore, if an ALJ declines to follow a policy in a particular case, the ALJ must explain the reasons why the policy was not followed. *See* 42 C.F.R. § 405.1062. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect. *See id.*

This Judge finds that the therapy in question has been proven to be safe and effective and is medically reasonable and necessary to treat this particular beneficiary's condition. This Judge explains his rationale as follows:

TTF Therapy Has Been Proven Safe and Effective Based on Authoritative Evidence

Because there is no NCD or LCD in effect on the dates of service at issue (E1399/A9999), this Judge must decide whether TTF has been proven safe and effective based on authoritative evidence. (*MPIM*, Ch. 13 at § 13.5.1; *MBPM*, Ch. 15 at § 110; *see also Almy*, 679 F.3d at 299). Such decisions should be based on either "published authoritative evidence" such as "definitive randomized clinical trials" or "general acceptance by the medical community," with the caveat that "[a]cceptance by individual health care providers" and "limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community." *MPIM* § 13.7.1; *see also Almy*, 679 F.3d at 300.

Based on the hearing testimony; medical evidence and studies submitted; NCCN Guidelines; and FDA approval of the device, this Judge finds that the device in question has been proven safe and effective based on authoritative evidence.

The record supports that recurrent glioblastoma multiforme is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. Recent clinical studies of the effect of treating GBM patients with TTF therapy with Temozolomide have shown significant improvements – approximately 50% – in survival rates. The safety and efficacy of TTF therapy is generally accepted in the medical community. After a thorough review of the clinical studies, this Judge finds the studies creditable in establishing the efficacy of TTF therapy in prolonging and improving the survival of patients diagnosed with GBM.

Finally, this Judge finds that the device is FDA approved, which is further evidence that it is “safe” and “effective.” Medicare law states that FDA clearance is *necessary*, but not *sufficient*, for Medicare coverage. (*Int’l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Specifically, FDA review seeks to determine whether a device is “safe and effective” such that it can be marketed to the general public. By contrast, Medicare coverage review seeks to determine whether the device is “reasonable and necessary” for treatment such that the device is worth the government’s money. (MBPM, ch. 15, § 110.1; *Int’l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Therefore, this Judge finds FDA approval to be further evidence of the device’s safety and effectiveness.

TTF Therapy is Medically Reasonable and Necessary to Treat this Particular Beneficiary’s Condition

This Judge finds the TTF therapy device at issue to be medically reasonable and necessary for the beneficiary because it is an appropriate treatment of the beneficiary’s condition and since there is no medically appropriate and realistically feasible alternative pattern of care for the beneficiary. (MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110).

First, this Judge takes into account the medical record and hearing testimony. The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by concomitant chemotherapy and radiation using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

The records indicate that [redacted] was a 57 year old male diagnosed with progressive left temporal glioblastoma that was supratentorial in location. (Ex. 1, pp. 21-24; Ex. 3, pp. 5-6, 9-11; Hearing CD.) The tumor was recurrent. (*Id.*) His treating physician recommended beginning TTF treatment on December 5, 2012, as the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (*Id.*)

The beneficiary’s medical records show that [redacted] initially was diagnosed with glioblastoma on February 27, 2007. (Ex. 1, pp. 21-24; Ex. 3, pp. 5-6, 9-11; Hearing CD.) He received concurrent radiation and chemotherapy with Temozolomide and Keppra after the first

surgery. (*Id.*) Due to another tumor progression, he had a second surgery on September 16, 2009. (*Id.*) He then received Temodar and Thalidomide until February 2012. (*Id.*) After a third craniotomy on March 9, 2013, he had a seizure involving his right side, face, and arm. (*Id.*) He also suffered from expressive aphasia as a result of the third surgery and mild comprehension difficulty. (*Id.*) Due to myelosuppression, his chemotherapy was put on hold. (*Id.*) Due to his recurrent glioblastoma, Mr. Calvillo's treating physician recommended that he begin TTF therapy on December 5, 2012. (*Id.*)

This Judge also takes into account the FDA approval letter, which sets forth specific criteria for beneficiaries who would be considered candidates for TTF therapy delivered by the Appellant:

This device is indicated for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically – or radiologically – confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy³, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 6, pp. 130-34.)

This Judge finds that the beneficiary meets all the criteria set forth by the FDA and the NCCN Guidelines.

Based on the foregoing evidence, this Judge finds that the TTF therapy device at issue has been proven to be safe and effective and is medically reasonable and necessary to treat the beneficiary's condition.

Conclusions of Law

Based upon the written evidence in the record and the testimony offered at the hearing, this Judge issues a **fully favorable** determination for Novocure Inc. Medicare coverage is appropriate under Medicare Part B for the NovoTTF-100A HCPCS code A9900 billed on April 23, 2013; June 5, 2013; and August 12, 2013 for . Coverage is supported by sufficient information as required by Sections 1862(a) and 1833(e) of the Social Security Act.

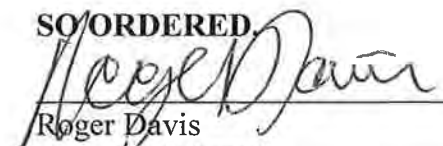
Order

The Medicare contractor is **DIRECTED** to process the claim in accordance with this decision.

APR 23 2013

Dated: _____

SO ORDERED


Roger Davis
U.S. Administrative Law Judge

³ This Judge notes that since this FDA approval letter dated April 8, 2011, the FDA has approved the Appellant's device* in combination with temozolomide for the treatment of adult patients with newly diagnosed GBM. See http://www.abta.org/about-us/news/brain-tumor-news/fda-approves-optune-in_oct15.html



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri**

Appeal of: Novocure Inc.	ALJ Appeal No.: 1-2556396529
Beneficiary: The Est. of	Medicare Part B
HICN: *****2832A	Before: Roger Davis U.S. Administrative Law Judge

DECISION

This Judge decides this appeal **fully favorable** to Novocure Inc. (the “Appellant”) after holding a telephonic hearing.

Findings of Fact

The Appellant seeks coverage of NovoTTF-100A HCPCS code E1399 billed on September 5, 2013 for treatment of progressive glioblastoma multiform (GBM)¹. This device is relatively new to cancer treatment. This non-invasive system is used in the beneficiary’s home, and delivers tumor treating fields therapy (TTF) to the brain to disrupt rapid cell division exhibited by recurrent GBM tumors. The system is comprised of a durable electrical field generator and disposable insulated transducer arrays (worn affixed to the scalp) for use with the portable generator. The system also includes lithium ion batteries, battery rack, battery charger, power supply, connection cables, and a carrying case. (Ex. 6, pp. 131-50.) The device is indicated for treatment of adult patients with histologically-confirmed glioblastoma multiforme, following histologically or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 6, pp. 120-24.)

¹ On January 1, 2014, CMS created a new code, E0766, to group all billing, including all components/supplies and monthly rental fees, for NovoTTF-100A. Prior to this new code, the Appellant used multiple miscellaneous codes to bill the items, including: A9999, A9900, E1399, and A4555. This Judge takes note of the different codes used to bill the device, but does not purport to dictate how or under which code payment should be affected and/or authorized. The legal analysis will address whether coverage is supported by the documentation submitted.

This device is manufactured by NovoCure, Ltd., and was approved by the Federal and Drug Administration (FDA) in April of 2011. (Ex. 6, pp. 120-24.) The device was approved after the pre-market approval pathway (PMA). This is the most rigorous medical device approval pathway, and is analogous to the FDA new drug pathway. The FDA approved the device on the basis of a multi-center randomized controlled pivotal (phase III) clinical trial. This was then followed by a positive vote from the FDA's independent Medical Device Advisory Committee's Neurological Devices Panel. (*Id.*) The device falls within the DME benefit category according to a July 26, 2013 letter from CMS. (Ex. 6, pg. 116.) The device is also included in the National Comprehensive Cancer Network Guidelines ("NCCN Guidelines") for recurrent glioblastoma, which is the standard of care for the diagnosis. The NCCN Guidelines are not binding in making Medicare coverage decisions. (Ex. 6, pp. 118-19.)

The beneficiary was a 57-year-old male diagnosed with recurrent glioblastoma multiforme progressive. (Ex. 1, pp. 17-20; Ex. 3, pp. 20-23; Hearing CD.) Glioblastomas (GBM) are tumors that arise from astrocytes—the star-shaped cells that make up the “glue-like,” or supportive tissue of the brain. These tumors are usually highly malignant because the cells reproduce quickly and they are supported by a large network of blood vessels. (*See* <http://www.abta.org/brain-tumor-information/types-of-tumors/glioblastoma.html>). Recurrent glioblastoma multiforme progressive is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. There are few, if any, available options that would benefit the patient in this clinical scenario. Patients with recurrent GBM have a one-year survival rate of approximately 10% and a median overall survival time of three to five months when not treated with an effective (active) therapy. (Ex. 6, pp. 131-50.)

The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by concomitant chemotherapy and radiation using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

The records indicate that [redacted] was a 57 year old male diagnosed with progressive left temporal glioblastoma that was supratentorial in location. (Ex. 1, pp. 17-20; Ex. 3, pp. 20-23; Hearing CD.) The tumor was recurrent. (*Id.*) His treating physician recommended beginning TTF treatment on December 5, 2012, as the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (*Id.*)

The beneficiary's medical records show that [redacted] initially was diagnosed with glioblastoma on February 27, 2007. (Ex. 1, pp. 17-20; Ex. 3, pp. 20-23; Hearing CD.) He received concurrent radiation and chemotherapy with Temozolomide and Keppra after the first surgery. (*Id.*) Due to another tumor progression, he had a second surgery on September 16, 2009. (*Id.*) He then received Temodar and Thalidomide until February 2012. (*Id.*) After a third craniotomy on March 9, 2013, he had a seizure involving his right side, face, and arm. (*Id.*) He

also suffered from expressive aphasia as a result of the third surgery and mild comprehension difficulty. (*Id.*) Due to myelosuppression, his chemotherapy was put on hold. (*Id.*) Due to his recurrent glioblastoma, treating physician recommended that he begin TTFields therapy on December 5, 2012. (*Id.*)

Procedural History

The Medicare Administrative Contractor denied coverage for the Part A medical equipment the Appellant billed. Then the Qualified Independent Contractor issued an unfavorable decision on the Appellant's appeal. Finally, the Appellant filed a request for a hearing before an Administrative Law Judge ("ALJ" or "Judge") with the Office of Medicare Hearings and Appeals ("OMHA").

This Judge conducted a hearing with representatives of the Appellant on March 16, 2018. All evidence was admitted, and accordingly, the administrative record is now closed.

Legal Framework

I. ALJ Review Authority

Health Plan enrollees who are dissatisfied with their Health Plan because they did not receive healthcare to which they believe they were entitled to, or because they contest the cost of a service they received, are entitled to an appeal process. Social Security Act § 1852(g), 42 U.S.C. § 1395w-22(g), 42 C.F.R. §§ 422.560, 422.562. The appeal process includes, if necessary, a hearing before an ALJ. 42 C.F.R. § 422.562(b)(4). An ALJ within the Office of Medicare Hearing and Appeals shall perform a *de novo* review of the case provided that there is a sufficient amount in controversy and that the appellant files the appeal in a timely fashion. 42 U.S.C. § 1395ff(b)(1)(A); *see also* 42 C.F.R. §§ 422.600, 405.1000 and 405.1002. *See generally* 70 Fed. Reg. 36386, 36387 (June 23, 2005) (delegation of Secretary's power specifically to OMHA to conduct reviews).

II. Principles of Law

I. ALJ Review Authority

A. Jurisdiction

Individuals or organizations dissatisfied with the reconsideration of an initial determination are entitled to hearings before the Secretary of the Department of Health and Human Services. There must be a sufficient amount in controversy at the time of the request for hearing, and the appellant must timely submit the request for hearing. (42 C.F.R. § 405.1014; Social Security Act ("the Act") § 1869(b)(1)(A)). The Secretary delegates OMHA to administer the nationwide hearings and appeals system, and the ALJs within OMHA issue the final decisions of the Secretary, unless later reviewed by the Medicare Appeals Council. (*See* 70 Fed. Reg. 36386, 36387 (June 23, 2005)).

The request for hearing is timely if the Appellant files within sixty days after they receive the QIC Reconsideration determination. (See 42 C.F.R. §405.1002(a)(1)).

For requests filed in calendar year 2013, the required minimum amount remaining in controversy for an ALJ hearing is \$140.00 (following application of any co-insurance or deductible). (42 C.F.R. § 405.1006(b)(1)).

B. Scope of Review

The issues before the ALJ include any issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. (42 C.F.R. § 405.1000; 405.1032).

C. Standard of Review

The ALJ conducts a *de novo* review and issues a decision based on the hearing record. (42 § C.F.R. § 405.1000(d)). *De novo* review requires the ALJ to evaluate the record and controlling laws and render an independent assessment without regard to prior determinations and findings on the claim. All laws and regulations pertaining to Medicare are binding on ALJs, including but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations.

The Appellant bears the burden of proving each element of a Medicare claim by a preponderance of the evidence. This is satisfied through the submission of sufficient evidence in accordance with Medicare rules. (See §§1814(a)(1), 1815(b), and 1833(e) of the Act; 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, 405.1030).

I. Principles of Law

A. Statutes and Regulations

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services (CMS). Section 1831 of the Act establishes the Supplemental Medical Insurance Program for the aged and disabled under Part B.

Section 1832 of the Act establishes the scope of benefits provided to beneficiaries under the Medicare Part B insurance program. Under Section 1832(a)(2)(B) of the Act, an individual is entitled to payment for medical and other health services furnished by a provider of services, or by others as arranged by the provider of services. (See also 42 C.F.R. §410.3). No payment shall be made to any provider under the Act unless the provider furnishes information to determine the amounts due to them for the period at issue. (See 42 C.F.R. § 424.5(a)(6); and Title XVIII, § 1833(e) of the Act).

Medicare will pay for services that are reasonable and medically necessary for the diagnosis or treatment of a condition, illness, or injury to the beneficiary, or to improve the functioning of a

malformed body member. (42 USC § 1395d(a)(1)). The provider must provide sufficient documentation to support the claim for payment. (42 C.F.R. § 424.5 (a)(6)).

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. Although not subject to the force and effect of law, CMS and its contractors have issued policy and guidelines describing the coverage criteria for selected types of medical services and supplies.

42 CFR Section 414.202 and the Chapter 15, Section 110.1 of the Medicare Benefit Policy Manual (CMS Publ. 100-2) provides, in relevant part, that durable medical equipment (“DME”) means equipment, furnished by a supplier or home health agency that –

- 1) Can withstand repeated use;
- 2) Is primarily and customarily used to serve a medical purpose;
- 3) Generally is not useful to an individual in the absence of an illness or injury; and
- 4) Is appropriate for use in the home.

Section 1879(a)(1) of Title XVIII of the Social Security Act provides in pertinent part, that when Medicare coverage is precluded under Section 1862(a)(1)(A) of the Act, i.e. the billed services were not reasonable and necessary, payment will be made, despite the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably been expected to know that the item was not covered. This is the limitation of liability provision. In other words, if either the beneficiary or the provider knew or had reason to know the service would not be covered, they are responsible for payment.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (“LMRPs”) or local coverage determinations (“LCDs”).

On the date of service at issue, no NCD or LCDs were in effect to enumerate coverage requirements for the medical device at issue.

Medically Reasonable and Necessary Medical Services

Part B of the Medicare Act extends coverage to certain types of durable medical equipment (DME) for qualified recipients. 42 U.S.C. § 1395k(a); *id.* § 1395x(s)(6). Not all DME is guaranteed coverage under Medicare Part B, however. The Medicare statute explicitly provides

that “no payment may be made under ... Part B of this subchapter for any expenses incurred for items ... [which] are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *Id.* § 1395y(a)(1)(A); *see also Almy v. Sebelius*, 679 F.3d 297, 299 (4th Cir. 2012).

Medicare coverage of DME is determined in one of three ways. First, Medicare issues a “national coverage determination” (NCD) binding throughout the Medicare system and not subject to review by administrative law judges. *Id.* § 1395ff(f)(1)(B). Second, one of the private insurance carriers with whom Medicare contracts to administer claims under Part B can issue a “local coverage determination” (LCD) “respecting whether or not a particular item or service is covered on an intermediary – or carrier-wide basis.” *Id.* § 1395ff(f)(2)(B); *see also Almy*, 679 F.3d at 299. Finally, if no NCD or LCD is in place, “contractors may make individual claim determinations,” including whether a particular DME meets the statutory requirement of being “reasonable and necessary.” 68 Fed. Reg. 63, 693.

Medicare also has developed guidance in the Medicare Program Integrity Manual (CMS Pub. 100-08) (MPIM), Ch. 13 at § 13.5.1, and the Medicare Benefit Policy Manual (CMS Pub. 100-02) (MBPM), Ch. 15 at § 110 for Medicare contractors applying the “reasonable and necessary” standard.² A device is not “reasonable and necessary” – and thus is not eligible for Medicare coverage – if it is:

- Not “safe” and “effective” – that is, if the device has not “been proven safe and effective based on authoritative evidence” or is not “generally accepted in the medical community as safe and effective for the condition for which it is used”;
- “[E]xperimental” – that is, “investigational”;
- Not “[a]ppropriate” for the individual beneficiary’s needs; or
- “[S]ubstantially more costly than a medically appropriate and realistically feasible alternative pattern of care.”

See also Almy, 679 F.3d at 299; *Int’l Rehabilitative Scis. Inc. v. Sebelius*, 688 F.3d 994, 997 (9th Cir. 2012).

The burden is on the claimant to show that the device is reasonable and necessary. *Almy*, 679 F.3d at 305.

Medicare also instructs contractors as to the type of evidence to be used in making these technical determinations. Such decisions should be based on either “published authoritative evidence” such as “definitive randomized clinical trials” or “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

² ALJs and the Medicare Appeals Council are not bound by CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. 42 C.F.R. § 405.1062(a).

Statement of the Issues

1. Whether all Medicare coverage requirements have been met warranting payment under Title XVIII of the Social Security Act?
2. Whether the limitation on liability provisions of Section 1879 are applicable?

Analysis

The crux of the issue in this appeal is whether the record establishes that the medical device at issue was medically reasonable and necessary for treatment of the beneficiary's condition. The Qualified Independent Contractor (QIC) denied coverage for the medical equipment, reasoning that the device had not been deemed a safe and effective treatment. The QIC found the Appellant liable for the non-covered charges. (Ex. 1, pp. 1-7.)

This Judge is aware that there is an LCD, specifically *CGS Admin., Local Coverage Determination L34665: Tumor Treatment Field Therapy (LCD L34665) (Oct. 2014)*. However, the LCD was not yet in effect on the dates of service at issue, and only summarily denies coverage stating that the device was not reasonable and necessary. This Judge also has reviewed three other LCD jurisdictions in search of further information and guidance, however, they provide no additional information. This Judge speculates that the LCDs lack details because the scientific evidence of the effectiveness of this therapy has only recently developed and the LCDs have not yet caught up with recent developments.

Pursuant to 42 C.F.R. § 405.1062, ALJs are not bound by LCDs, but will give substantial deference to these policies if they are applicable to a particular case. Furthermore, if an ALJ declines to follow a policy in a particular case, the ALJ must explain the reasons why the policy was not followed. *See* 42 C.F.R. § 405.1062. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect. *See id.*

This Judge finds that the therapy in question has been proven to be safe and effective and is medically reasonable and necessary to treat this particular beneficiary's condition. This Judge explains his rationale as follows:

TTF Therapy Has Been Proven Safe and Effective Based on Authoritative Evidence

Because there is no NCD or LCD in effect on the dates of service at issue (E1399/A9999), this Judge must decide whether TTF has been proven safe and effective based on authoritative evidence. (*MPIM*, Ch. 13 at § 13.5.1; *MBPM*, Ch. 15 at § 110; *see also Almy*, 679 F.3d at 299). Such decisions should be based on either "published authoritative evidence" such as "definitive randomized clinical trials" or "general acceptance by the medical community," with the caveat that "[a]cceptance by individual health care providers" and "limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community." *MPIM* § 13.7.1; *see also Almy*, 679 F.3d at 300.

Based on the hearing testimony; medical evidence and studies submitted; NCCN Guidelines; and FDA approval of the device, this Judge finds that the device in question has been proven safe and effective based on authoritative evidence.

The record supports that recurrent glioblastoma multiforme is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. Recent clinical studies of the effect of treating GBM patients with TTF therapy with Temozolomide have shown significant improvements – approximately 50% – in survival rates. The safety and efficacy of TTF therapy is generally accepted in the medical community. After a thorough review of the clinical studies, this Judge finds the studies creditable in establishing the efficacy of TTF therapy in prolonging and improving the survival of patients diagnosed with GBM.

Finally, this Judge finds that the device is FDA approved, which is further evidence that it is “safe” and “effective.” Medicare law states that FDA clearance is *necessary*, but not *sufficient*, for Medicare coverage. (*Int’l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Specifically, FDA review seeks to determine whether a device is “safe and effective” such that it can be marketed to the general public. By contrast, Medicare coverage review seeks to determine whether the device is “reasonable and necessary” for treatment such that the device is worth the government’s money. (MBPM, ch. 15, § 110.1; *Int’l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Therefore, this Judge finds FDA approval to be further evidence of the device’s safety and effectiveness.

TTF Therapy is Medically Reasonable and Necessary to Treat this Particular Beneficiary’s Condition

This Judge finds the TTF therapy device at issue to be medically reasonable and necessary for the beneficiary because it is an appropriate treatment of the beneficiary’s condition and since there is no medically appropriate and realistically feasible alternative pattern of care for the beneficiary. (MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110).

First, this Judge takes into account the medical record and hearing testimony. The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by concomitant chemotherapy and radiation using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

The records indicate that [redacted] was a 57 year old male diagnosed with progressive left temporal glioblastoma that was supratentorial in location. (Ex. 1, pp. 17-20; Ex. 3, pp. 20-23; Hearing CD.) The tumor was recurrent. (*Id.*) His treating physician recommended beginning TTF treatment on December 5, 2012, as the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (*Id.*)

The beneficiary’s medical records show that [redacted] initially was diagnosed with glioblastoma on February 27, 2007. (Ex. 1, pp. 17-20; Ex. 3, pp. 20-23; Hearing CD.) He received concurrent radiation and chemotherapy with Temozolomide and Keppra after the first

surgery. (*Id.*) Due to another tumor progression, he had a second surgery on September 16, 2009. (*Id.*) He then received Temodar and Thalidomide until February 2012. (*Id.*) After a third craniotomy on March 9, 2013, he had a seizure involving his right side, face, and arm. (*Id.*) He also suffered from expressive aphasia as a result of the third surgery and mild comprehension difficulty. (*Id.*) Due to myelosuppression, his chemotherapy was put on hold. (*Id.*) Due to his recurrent glioblastoma, treating physician recommended that he begin TTFields therapy on December 5, 2012. (*Id.*)

This Judge also takes into account the FDA approval letter, which sets forth specific criteria for beneficiaries who would be considered candidates for TTF therapy delivered by the Appellant:

This device is indicated for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically – or radiologically – confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy³, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 6, pp. 120-24.)

This Judge finds that the beneficiary meets all the criteria set forth by the FDA and the NCCN Guidelines.

Based on the foregoing evidence, this Judge finds that the TTF therapy device at issue has been proven to be safe and effective and is medically reasonable and necessary to treat the beneficiary's condition.

Conclusions of Law

Based upon the written evidence in the record and the testimony offered at the hearing, this Judge issues a **fully favorable** determination for Novocure Inc. Medicare coverage is appropriate under Medicare Part B for the NovoTTF-100A HCPCS code E1399 billed on September 5, 2013 for Coverage is supported by sufficient information as required by Sections 1862(a) and 1833(e) of the Social Security Act.


Order

The Medicare contractor is **DIRECTED** to process the claim in accordance with this decision.

APR 23 2018

Dated: _____

SO ORDERED.


Roger Davis

U.S. Administrative Law Judge

³ This Judge notes that since this FDA approval letter dated April 8, 2011, the FDA has approved the Appellant's device* in combination with temozolomide for the treatment of adult patients with newly diagnosed GBM. See http://www.abta.org/about-us/news/brain-tumor-news/fda-approves-optune-in_oct15.html



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri**

Appeal of: Novocure Inc.	ALJ Appeal No.: 1-2571331126
Beneficiary: The Estate of	Medicare Part B
HICN: *****4696A	Before: Roger Davis U.S. Administrative Law Judge

DECISION

This Judge decides this appeal **fully favorable** to Novocure Inc. (the “Appellant”) after holding a telephonic hearing.

Findings of Fact

The Appellant seeks coverage of NovoTTF-100A HCPCS code E1399 billed on July 21, 2013 and August 21, 2013; and HCPCS code A9999 billed on June 19, 2013; July 22, 2013; and August 19, 2013 for treatment of progressive glioblastoma multiform (GBM)¹. This device is relatively new to cancer treatment. This non-invasive system is used in the beneficiary’s home, and delivers tumor treating fields therapy (TTF) to the brain to disrupt rapid cell division exhibited by recurrent GBM tumors. The system is comprised of a durable electrical field generator and disposable insulated transducer arrays (worn affixed to the scalp) for use with the portable generator. The system also includes lithium ion batteries, battery rack, battery charger, power supply, connection cables, and a carrying case. (Ex. 2, pp. 15-20). The device is indicated for treatment of adult patients with histologically-confirmed glioblastoma multiforme, following histologically or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 2, p. 4).

¹ On January 1, 2014, CMS created a new code, E0766, to group all billing, including all components/supplies and monthly rental fees, for NovoTTF-100A. Prior to this new code, the Appellant used multiple miscellaneous codes to bill the items, including: A9999, A9900, E1399, and A4555. This Judge takes note of the different codes used to bill the device, but does not purport to dictate how or under which code payment should be affected and/or authorized. The legal analysis will address whether coverage is supported by the documentation submitted.

This device is manufactured by NovoCure, Ltd., and was approved by the Federal and Drug Administration (FDA) in April of 2011. (Ex. 2, pp. 4-8). The device was approved after the pre-market approval pathway (PMA). This is the most rigorous medical device approval pathway, and is analogous to the FDA new drug pathway. The FDA approved the device on the basis of a multi-center randomized controlled pivotal (phase III) clinical trial. This was then followed by a positive vote from the FDA's independent Medical Device Advisory Committee's Neurological Devices Panel. (*Id.*). The device falls within the DME benefit category according to a July 26, 2013 letter from CMS. (Ex. 6, p. 137) The device is also included in the National Comprehensive Cancer Network Guidelines ("NCCN Guidelines") for recurrent glioblastoma, which is the standard of care for the diagnosis. The NCCN Guidelines are not binding in making Medicare coverage decisions. (Ex. 2, pp. 1-3).

The beneficiary is a 67-year-old male diagnosed with unresectable, recurrent glioblastoma multiforme progressive. (Ex. 3, pp. 1, 2, 25, 57). Glioblastomas (GBM) are tumors that arise from astrocytes—the star-shaped cells that make up the “glue-like,” or supportive tissue of the brain. These tumors are usually highly malignant because the cells reproduce quickly and they are supported by a large network of blood vessels. (See <http://www.abta.org/brain-tumor-information/types-of-tumors/glioblastoma.html>). Recurrent glioblastoma multiforme progressive is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. There are few, if any, available options that would benefit the patient in this clinical scenario. Patients with recurrent GBM have a one-year survival rate of approximately 10% and a median overall survival time of three to five months when not treated with an effective (active) therapy. (Ex. 2, pp. 25-26).

The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by contaminant chemotherapy and radiation using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

The records indicate the beneficiary's glioblastoma was unresectable, and was supratentorial in location. (Ex. 3, p. 25; and Hearing CD). The tumor was recurrent and rated Grade 4. (Ex. 3, p. 57). His treating physician recommended beginning TTF treatment on May 21, 2013, as the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (Ex. 1, pp. 39-40).

The beneficiary's medical records document that he initially presented with partial seizures in December 2011. An initial assessment performed January 17, 2012 confirmed the mass as a low-grade glioma. The beneficiary received initial infusion Avastin (chemotherapy) on March 21, 2012; and Tremodar (additional chemotherapy) and radiation therapy in early April 2012. On April 25, 2012 Avastin was held and Bactrim was started due to a localized scalp infection. Tremodar was initially completed May 30, 2012, and then restarted on June 14, 2012. The

treating oncologist continued to monitor the beneficiary's disease progression via MRIs, and ultimately ordered the Novo TTF placement on May 21, 2013. (Ex. 3, pp. 16-73). As of an August 20, 2013 office visit, the beneficiary "continued to do remarkably well clinically." His functional mental status remained excellent, he had progressive episodes of facial and tooth numbness, but maintained good appetite with no headaches, fevers, or chills. His only complaint was short-term memory, and infrequent/sporadic seizures. The records indicate he wore the NovoTTF device 24 hours per day, taking it off only on Sundays for a few hours when using the restroom. He remained fairly active, and would sometimes drive his truck or tractor around his property for fun. (Ex. 3, pp. 2-3).

Procedural History

The Medicare Administrative Contractor denied coverage for the Part A medical equipment the Appellant billed. Then the Qualified Independent Contractor issued an unfavorable decision on the Appellant's appeal. Finally, the Appellant filed a request for a hearing before an Administrative Law Judge ("ALJ" or "Judge") with the Office of Medicare Hearings and Appeals ("OMHA").

This Judge conducted a hearing with representatives of the Appellant on February 16, 2018. All evidence was admitted, and accordingly, the administrative record is now closed.

Legal Framework

I. ALJ Review Authority

Health Plan enrollees who are dissatisfied with their Health Plan because they did not receive healthcare to which they believe they were entitled to, or because they contest the cost of a service they received, are entitled to an appeal process. Social Security Act § 1852(g), 42 U.S.C. § 1395w-22(g), 42 C.F.R. §§ 422.560, 422.562. The appeal process includes, if necessary, a hearing before an ALJ. 42 C.F.R. § 422.562(b)(4). An ALJ within the Office of Medicare Hearing and Appeals shall perform a *de novo* review of the case provided that there is a sufficient amount in controversy and that the appellant files the appeal in a timely fashion. 42 U.S.C. § 1395ff(b)(1)(A); *see also* 42 C.F.R. §§ 422.600, 405.1000 and 405.1002. *See generally* 70 Fed. Reg. 36386, 36387 (June 23, 2005) (delegation of Secretary's power specifically to OMHA to conduct reviews).

II. Principles of Law

I. ALJ Review Authority

A. Jurisdiction

Individuals or organizations dissatisfied with the reconsideration of an initial determination are entitled to hearings before the Secretary of the Department of Health and Human Services. There must be a sufficient amount in controversy at the time of the request for hearing, and the appellant must timely submit the request for hearing. (42 C.F.R. § 405.1014; Social Security Act

("the Act") § 1869(b)(1)(A)). The Secretary delegates OMHA to administer the nationwide hearings and appeals system, and the ALJs within OMHA issue the final decisions of the Secretary, unless later reviewed by the Medicare Appeals Council. (See 70 Fed. Reg. 36386, 36387 (June 23, 2005)).

The request for hearing is timely if the Appellant files within sixty days after they receive the QIC Reconsideration determination. (See 42 C.F.R. §405.1002(a)(1)).

For requests filed in calendar year 2013, the required minimum amount remaining in controversy for an ALJ hearing is \$140.00 (following application of any co-insurance or deductible). (42 C.F.R. § 405.1006(b)(1)).

B. Scope of Review

The issues before the ALJ include any issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. (42 C.F.R. § 405.1000; 405.1032).

C. Standard of Review

The ALJ conducts a *de novo* review and issues a decision based on the hearing record. (42 § C.F.R. § 405.1000(d)). *De novo* review requires the ALJ to evaluate the record and controlling laws and render an independent assessment without regard to prior determinations and findings on the claim. All laws and regulations pertaining to Medicare are binding on ALJs, including but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations.

The Appellant bears the burden of proving each element of a Medicare claim by a preponderance of the evidence. This is satisfied through the submission of sufficient evidence in accordance with Medicare rules. (See §§1814(a)(1), 1815(b), and 1833(e) of the Act; 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, 405.1030).

I. Principles of Law

A. Statutes and Regulations

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services (CMS). Section 1831 of the Act establishes the Supplemental Medical Insurance Program for the aged and disabled under Part B.

Section 1832 of the Act establishes the scope of benefits provided to beneficiaries under the Medicare Part B insurance program. Under Section 1832(a)(2)(B) of the Act, an individual is entitled to payment for medical and other health services furnished by a provider of services, or by others as arranged by the provider of services. (See also 42 C.F.R. §410.3). No payment shall be made to any provider under the Act unless the provider furnishes information to determine the

amounts due to them for the period at issue. (See 42 C.F.R. § 424.5(a)(6); and Title XVIII, § 1833(e) of the Act).

Medicare will pay for services that are reasonable and medically necessary for the diagnosis or treatment of a condition, illness, or injury to the beneficiary, or to improve the functioning of a malformed body member. (42 USC § 1395d(a)(1)). The provider must provide sufficient documentation to support the claim for payment. (42 C.F.R. § 424.5 (a)(6)).

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. Although not subject to the force and effect of law, CMS and its contractors have issued policy and guidelines describing the coverage criteria for selected types of medical services and supplies.

42 CFR Section 414.202 and the Chapter 15, Section 110.1 of the Medicare Benefit Policy Manual (CMS Publ. 100-2) provides, in relevant part, that durable medical equipment ("DME") means equipment, furnished by a supplier or home health agency that –

- 1) Can withstand repeated use;
- 2) Is primarily and customarily used to serve a medical purpose;
- 3) Generally is not useful to an individual in the absence of an illness or injury; and
- 4) Is appropriate for use in the home.

Section 1879(a)(1) of Title XVIII of the Social Security Act provides in pertinent part, that when Medicare coverage is precluded under Section 1862(a)(1)(A) of the Act, i.e. the billed services were not reasonable and necessary, payment will be made, despite the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably been expected to know that the item was not covered. This is the limitation of liability provision. In other words, if either the beneficiary or the provider knew or had reason to know the service would not be covered, they are responsible for payment.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies ("LMRPs") or local coverage determinations ("LCDs").

On the date of service at issue, no NCD or LCDs were in effect to enumerate coverage requirements for the medical device at issue.

Medically Reasonable and Necessary Medical Services

Part B of the Medicare Act extends coverage to certain types of durable medical equipment (DME) for qualified recipients. 42 U.S.C. § 1395k(a); *id.* § 1395x(s)(6). Not all DME is guaranteed coverage under Medicare Part B, however. The Medicare statute explicitly provides that “no payment may be made under ... Part B of this subchapter for any expenses incurred for items ... [which] are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *Id.* § 1395y(a)(1)(A); *see also Almy v. Sebelius*, 679 F.3d 297, 299 (4th Cir. 2012).

Medicare coverage of DME is determined in one of three ways. First, Medicare issues a “national coverage determination” (NCD) binding throughout the Medicare system and not subject to review by administrative law judges. *Id.* § 1395ff(f)(1)(B). Second, one of the private insurance carriers with whom Medicare contracts to administer claims under Part B can issue a “local coverage determination” (LCD) “respecting whether or not a particular item or service is covered on an intermediary – or carrier-wide basis.” *Id.* § 1395ff(f)(2)(B); *see also Almy*, 679 F.3d at 299. Finally, if no NCD or LCD is in place, “contractors may make individual claim determinations,” including whether a particular DME meets the statutory requirement of being “reasonable and necessary.” 68 Fed. Reg. 63, 693.

Medicare also has developed guidance in the Medicare Program Integrity Manual (CMS Pub. 100-08) (MPIM), Ch. 13 at § 13.5.1, and the Medicare Benefit Policy Manual (CMS Pub. 100-02) (MBPM), Ch. 15 at § 110 for Medicare contractors applying the “reasonable and necessary” standard.² A device is not “reasonable and necessary” – and thus is not eligible for Medicare coverage – if it is:

- Not “safe” and “effective” – that is, if the device has not “been proven safe and effective based on authoritative evidence” or is not “generally accepted in the medical community as safe and effective for the condition for which it is used”;
- “[E]xperimental” – that is, “investigational”;
- Not “[a]ppropriate” for the individual beneficiary’s needs; or
- “[S]ubstantially more costly than a medically appropriate and realistically feasible alternative pattern of care.”

See also Almy, 679 F.3d at 299; *Int’l Rehabilitative Scis. Inc. v. Sebelius*, 688 F.3d 994, 997 (9th Cir. 2012).

The burden is on the claimant to show that the device is reasonable and necessary. *Almy*, 679 F.3d at 305.

Medicare also instructs contractors as to the type of evidence to be used in making these technical determinations. Such decisions should be based on either “published authoritative evidence” such as “definitive randomized clinical trials” or “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and

² ALJs and the Medicare Appeals Council are not bound by CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. 42 C.F.R. § 405.1062(a).

“limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

Statement of the Issues

1. Whether all Medicare coverage requirements have been met warranting payment under Title XVIII of the Social Security Act?
2. Whether the limitation on liability provisions of Section 1879 are applicable?

Analysis

The crux of the issue in this appeal is whether the record establishes that the medical device at issue was medically reasonable and necessary for treatment of the beneficiary's condition. The Qualified Independent Contractor (QIC) denied coverage for the medical equipment, reasoning that the device had not been deemed a safe and effective treatment. The QIC found the Appellant liable for the non-covered charges. (Ex. 1, pp. 2-6).

This Judge is aware that there is an LCD, specifically *CGS Admin., Local Coverage Determination L34665: Tumor Treatment Field Therapy (LCD L34665) (Oct. 2014)*. However, the LCD was not yet in effect on the dates of service at issue, and only summarily denies coverage stating that the device was not reasonable and necessary. This Judge also has reviewed three other LCD jurisdictions in search of further information and guidance, however, they provide no additional information. This Judge speculates that the LCDs lack details because the scientific evidence of the effectiveness of this therapy has only recently developed and the LCDs have not yet caught up with recent developments.

Pursuant to 42 C.F.R. § 405.1062, ALJs are not bound by LCDs, but will give substantial deference to these policies if they are applicable to a particular case. Furthermore, if an ALJ declines to follow a policy in a particular case, the ALJ must explain the reasons why the policy was not followed. *See* 42 C.F.R. § 405.1062. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect. *See id.*

This Judge finds that the therapy in question has been proven to be safe and effective and is medically reasonable and necessary to treat this particular beneficiary's condition. This Judge explains his rationale as follows:

TTF Therapy Has Been Proven Safe and Effective Based on Authoritative Evidence

Because there is no NCD or LCD in effect on the dates of service at issue (E1399/A9999), this Judge must decide whether TTF has been proven safe and effective based on authoritative evidence. (MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110; *see also Almy*, 679 F.3d at 299). Such decisions should be based on either “published authoritative evidence” such as “definitive randomized clinical trials” or “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

Based on the hearing testimony; medical evidence and studies submitted; NCCN Guidelines; and FDA approval of the device, this Judge finds that the device in question has been proven safe and effective based on authoritative evidence.

The record supports that recurrent glioblastoma multiforme is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. Recent clinical studies of the effect of treating GBM patients with TTF therapy with Temozolomide have shown significant improvements – approximately 50% – in survival rates. The safety and efficacy of TTF therapy is generally accepted in the medical community. After a thorough review of the clinical studies, this Judge finds the studies creditable in establishing the efficacy of TTF therapy in prolonging and improving the survival of patients diagnosed with GBM.

Finally, this Judge finds that the device is FDA approved, which is further evidence that it is “safe” and “effective.” Medicare law states that FDA clearance is *necessary*, but not *sufficient*, for Medicare coverage. (*Int’l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Specifically, FDA review seeks to determine whether a device is “safe and effective” such that it can be marketed to the general public. By contrast, Medicare coverage review seeks to determine whether the device is “reasonable and necessary” for treatment such that the device is worth the government’s money. (MBPM, ch. 15, § 110.1; *Int’l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Therefore, this Judge finds FDA approval to be further evidence of the device’s safety and effectiveness.

TTF Therapy is Medically Reasonable and Necessary to Treat this Particular Beneficiary’s Condition

This Judge finds the TTF therapy device at issue to be medically reasonable and necessary for the beneficiary because it is an appropriate treatment of the beneficiary’s condition and since there is no medically appropriate and realistically feasible alternative pattern of care for the beneficiary. (MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110).

First, this Judge takes into account the medical record and hearing testimony. The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by contaminant chemotherapy and radiation using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

The records indicate the beneficiary’s glioblastoma was unresectable, and was supratentorial in location. (Ex. 3, p. 25; and Hearing CD). The tumor was recurrent and rated Grade 4. (Ex. 3, p. 57). His treating physician recommended beginning TTF treatment on May 21, 2013, as the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (Ex. 1, pp. 39-40).

The beneficiary's medical records document that he initially presented with partial seizures in December 2011. An initial assessment performed January 17, 2012 confirmed the mass as a low-grade glioma. The beneficiary received initial infusion Avastin (chemotherapy) on March 21, 2012; and Tremodar (additional chemotherapy) and radiation therapy in early April 2012. On April 25, 2012 Avastin was held and Bactrim was started due to localized scalp infection. Tremodar was initially completed May 30, 2012, and then restarted on June 14, 2012. The treating oncologist continued to monitor the beneficiary's disease progression via MRIs, and ultimately ordered the Novo TTF placement on May 21, 2013. (Ex. 3, pp. 16-73). As of an August 20, 2013 office visit, the beneficiary "continued to do remarkably well clinically." His functional mental status remained excellent, he had progressive episodes of facial and tooth numbness, but maintained good appetite with no headaches, fevers, or chills. His only complaint was short-term memory, and infrequent/sporadic seizures. The records indicate he wore the NovoTTF device 24 hours per day, taking it off only on Sundays for a few hours when using the restroom. He remained fairly active, and would sometimes drive his truck or tractor around his property for fun. (Ex. 3, pp. 2-3).

This Judge also takes into account the FDA approval letter, which sets forth specific criteria for beneficiaries who would be considered candidates for TTF therapy delivered by the Appellant:

This device is indicated for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically – or radiologically – confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy³, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 2, pp. 4-8.)

This Judge finds that the beneficiary meets all the criteria set forth by the FDA and the NCCN Guidelines.

Based on the foregoing evidence, this Judge finds that the TTF therapy device at issue has been proven to be safe and effective and is medically reasonable and necessary to treat the beneficiary's condition.

³ This Judge notes that since this FDA approval letter dated April 8, 2011, the FDA has approved the Appellant's device* in combination with temozolomide for the treatment of adult patients with newly diagnosed GBM. See http://www.abta.org/about-us/news/brain-tumor-news/fda-approves-optune-in_oct15.html

Conclusions of Law


Based upon the written evidence in the record and the testimony offered at the hearing, this Judge issues a **fully favorable** determination for Novocure Inc. Medicare coverage is appropriate under Medicare Part B for the NovoTTF-100A HCPCS code E1399 billed on July 21, 2013 and August 21, 2013; and HCPCS code A9999 billed on June 19, 2013; July 22, 2013; and August 19, 2013 for C. Ritchie. Coverage is supported by sufficient information as required by Sections 1862(a) and 1833(e) of the Social Security Act.

Order

The Medicare contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: APR 09 2018



Roger Davis
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri

Appeal of: REDACTED

ALJ Appeal No.: REDACTED

Beneficiary: REDACTED

Medicare Part C

HICN: *****0013A

Before: **Roger Davis**
U.S. Administrative Law Judge

DECISION

This Judge decides this appeal favorable to REDACTED (the “Appellant”) after holding a hearing.

Findings of Fact

The beneficiary and appellant, REDACTED is enrolled in a health plan (the Health Plan”) that is offered by Humana, a Medicare Advantage Organization (MAO). REDACTED is seeking pre-approval from the Health Plan for coverage of Optune for treatment of his glioblastoma (current procedural terminology (CPT) code E0766). Optune is a relatively new approach to cancer treatment which uses tumor treating fields (TTFields) to interfere with the division of malignant cells. (Ex. 3, pp. 2-3.) TTFields therapy is a locally or regionally delivered treatment that uses alternating electric fields to disrupt the rapid cell division exhibited by cancer cells. (*Id.*) Patients treated with TTFields wear insulated transducer arrays on the scalp attached to the portable field generator. (*Id.*)

This device is manufactured by NovoCure, Ltd., and was approved by the Federal and Drug Administration (FDA) in April of 2011. (Ex. 3, pp. 110-14.)

REDACTED is a year old gentleman who is diagnosed with glioblastoma. Glioblastomas (GBM) are tumors that arise from astrocytes—the star-shaped cells that make up the “glue-like,” or supportive tissue of the brain. These tumors are usually highly malignant (cancerous) because the cells reproduce quickly and they are supported by a large network of blood vessels. See <http://www.abta.org/brain-tumor-information/types-of-tumors/glioblastoma.html>.

REDACTED presented with speech difficulty in July of 2015. (Ex. 3, pp. 2-3; Hearing CD.) An MRI revealed a mass in the left lateral temporal lobe. (*Id.*) On August 10, 2015, he underwent a

craniotomy¹ with pathology confirming GBM. (*Id.*) Dr. [REDACTED] [REDACTED] treating physician, testified that during the surgery he was able to remove most of the tumor. (*Id.*) Dr. [REDACTED] testified that following surgery, most patients relapse, and therefore they are started on radiation therapy with concurrent chemotherapy medication called Temozolomide. (*Id.*) [REDACTED] received five weeks of radiation therapy and is currently taking Temozolomide. (*Id.*)

Dr. [REDACTED] stated that recurrent glioblastoma multiforme is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. (Ex. 3, pg. 5; Hearing CD.) He stated that he has been treating brain tumors for thirty years and the treatment course described above of radiation therapy with Temozolomide has made an insignificant improvement in survival rates. (*Id.*) He testified that recent clinical studies of the effect of treating GBM patients with TTFields therapy with Temozolomide have shown significant improvements – approximately 50% – in survival rates. (*Id.*)

Dr. [REDACTED] also stated that [REDACTED] has failed systemic surgery, chemotherapy and all radiotherapy options approved for this clinical scenario. (*Id.*) Therefore, he certified that “there are few if any available options that would benefit the patient in this clinical scenario.” (*Id.*) He certified that “Optune is currently the only chronic treatment option for recurrent glioblastoma that has established its survival benefit and safety profile in a randomized controlled trial against a control arm receiving active effective therapy.” (*Id.*)

Mr. Dan McCoy, [REDACTED] representative who is affiliated with NovoCure, testified that the Health Plan has paid for this therapy for GBM patients in the past. (Hearing CD.) He also testified that there are approximately 230 treatment sites in the country with physicians who are certified to prescribe the therapy in question. (*Id.*)

Procedural History

[REDACTED] sought pre-approval from his health plan for coverage of Optune (TTFields therapy) for treatment of his glioblastoma. The Health Plan denied coverage for the treatment citing *NHIC Corp., Local Coverage Determination L34823: Tumor Treatment Field Therapy (LCD L34823) (Oct. 2015)*, which states that “Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.” (Ex. 1, pg. 13.) The Health Plan forwarded the appeal to MAXIMUS Federal Services, the Medicare Part C Qualified Independent Contractor (QIC), which also denied coverage of the treatment at issue citing to L34823. [REDACTED] then filed a request for a hearing before an Administrative Law Judge (ALJ) in the Office of Medicare Hearings and Appeals (OMHA).

This Judge conducted a hearing with the following participants on December 16, 2015: Dr. [REDACTED] (treating physician); [REDACTED] (daughter); Mr. Dan McCoy ([REDACTED] representative, affiliated with NovoCure); and Ms. Cynthia McCloud (a representative of the Health Plan).

¹ A craniotomy is the surgical removal of part of the bone from the skull to expose the brain. Specialized tools are used to remove the section of bone called the bone flap. The bone flap is temporarily removed, then replaced after the brain surgery has been performed. See http://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/brain_tumor/treatment/surgery/craniotomy.html

Legal Framework

I. ALJ Review Authority

Health Plan enrollees who are dissatisfied with their Health Plan because they did not receive healthcare to which they believe they were entitled to, or because they contest the cost of a service they received, are entitled to an appeal process. Social Security Act § 1852(g), 42 U.S.C. § 1395w-22(g), 42 C.F.R. §§ 422.560, 422.562. The appeal process includes, if necessary, a hearing before an ALJ. 42 C.F.R. § 422.562(b)(4). An ALJ within the Office of Medicare Hearing and Appeals shall perform a *de novo* review of the case provided that there is a sufficient amount in controversy and that the appellant files the appeal in a timely fashion. 42 U.S.C. § 1395ff(b)(1)(A); *see also* 42 C.F.R. §§ 422.600, 405.1000 and 405.1002. *See generally* 70 Fed. Reg. 36386, 36387 (June 23, 2005) (delegation of Secretary's power specifically to OMHA to conduct reviews).

II. Principles of Law

Managed Care Organizations

A managed care organization (MAO) offering a Medicare Advantage (MA) plan must provide enrollees with “basic benefits,” which are all items and services covered by Medicare Part A and Part B available to beneficiaries residing in the plan’s service area. 42 C.F.R. § 422.101(a). An MA plan “must provide enrollees in that plan with coverage of the basic benefits by furnishing the benefits directly or through arrangements, or by paying for the benefits.” 42 C.F.R. § 422.100(a). In providing “basic benefits,” an MAO must comply with national coverage determinations (NCDs) issued by CMS, “[g]eneral coverage guidelines included in original Medicare manuals and instructions unless superseded by operational policy letters or regulations in [part 422] or related instructions; and . . . [w]ritten coverage decisions of local Medicare contractors.” 42 C.F.R. § 422.101(b). At its discretion, an MA plan may also offer additional (or “supplemental”) benefits beyond those covered by original Medicare. 42 C.F.R. § 422.102.

Medically Reasonable and Necessary Medical Services

Part B of the Medicare Act extends coverage to certain types of durable medical equipment (DME) for qualified recipients. 42 U.S.C. § 1395k(a); *id.* § 1395x(s)(6). Not all DME is guaranteed coverage under Medicare Part B, however. The Medicare statute explicitly provides that “no payment may be made under ... Part B of this subchapter for any expenses incurred for items ... [which] are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *Id.* § 1395y(a)(1)(A); *see also Almy v. Sebelius*, 679 F.3d 297, 299 (4th Cir. 2012).

Medicare coverage of DME is determined in one of three ways. First, Medicare issues a “national coverage determination” (NCD) binding throughout the Medicare system and not subject to review by administrative law judges. *Id.* § 1395ff(f)(1)(B). Second, one of the private insurance carriers with whom Medicare contracts to administer claims under Part B can issue a “local coverage determination” (LCD) “respecting whether or not a particular item or service is covered on an intermediary – or carrier-wide basis.” *Id.* § 1395ff(f)(2)(B); *see also Almy*, 679

F.3d at 299. Finally, if no NCD or LCD is in place, “contractors may make individual claim determinations,” including whether a particular DME meets the statutory requirement of being “reasonable and necessary.” 68 Fed. Reg. 63, 693.

Medicare also has developed guidance in the Medicare Program Integrity Manual (CMS Pub. 100-08) (MPIM), Ch. 13 at § 13.5.1, and the Medicare Benefit Policy Manual (CMS Pub. 100-02) (MBPM), Ch. 15 at § 110 for Medicare contractors applying the “reasonable and necessary” standard.² A device is not “reasonable and necessary” – and thus is not eligible for Medicare coverage – if it is:

- Not “safe” and “effective” – that is, if the device has not “been proven safe and effective based on authoritative evidence” or is not “generally accepted in the medical community as safe and effective for the condition for which it is used”;
- “[E]xperimental” – that is, “investigational”;
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- “[S]ubstantially more costly than a medically appropriate and realistically feasible alternative pattern of care.”

See also Almy, 679 F.3d at 299; *Int’l Rehabilitative Scis. Inc. v. Sebelius*, 688 F.3d 994, 997 (9th Cir. 2012).

The burden is on the claimant to show that the device is reasonable and necessary. *Almy*, 679 F.3d at 305.

Medicare also instructs contractors as to the type of evidence to be used in making these technical determinations. Such decisions should be based on either “published authoritative evidence” such as “definitive randomized clinical trials” or “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

Statement of the Issues

The issue on appeal is whether the Health Plan is required to pre-approve coverage for Optune (TTFields therapy) for treatment of REDACTED glioblastoma.

Analysis

In this appeal, REDACTED is seeking pre-approval from the Health Plan for coverage of Optune (TTFields therapy) for treatment of his glioblastoma.

The QIC denied coverage for the therapy at issue stating that:

² ALJs and the Medicare Appeals Council are not bound by CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. 42 C.F.R. § 405.1062(a).

Humana must follow Medicare rules. The rules [LCD L34823] say that tumor treatment field therapy is not reasonable and necessary. (Ex. 1, pg. 4.)

According to the terms of the Health Plan, it provides coverage of services to its members based on the coverage guidelines established by Medicare. (Ex. 2, pg. 28.) Specifically, in order to be covered under the Health Plan, the equipment at issue must be deemed as medically reasonable and necessary under Medicare guidelines. (*Id.*) The Health Plan specifies that in order to be deemed “medically necessary,” services, supplies, or drugs must be “needed for the prevention, diagnosis, or treatment of your medical condition and meet accepted standards of medical practice.” (*Id.*)

After carefully reviewing the evidence submitted and listening to the hearing testimony, this Judge concludes that the Health Plan must pay for the TTFields therapy in question. This Judge is aware that there is a relevant LCD, specifically *NHIC Corp., Local Coverage Determination L34823: Tumor Treatment Field Therapy (LCD L34823) (Oct. 2015)*, which simply states that “Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.” This LCD provides no additional guidelines, criteria for application, or reasoning. This Judge also has reviewed five other LCDs for other jurisdictions in search of further guidelines, however, they provide no additional information. This Judge speculates that the LCDs lack details because the scientific evidence of the effectiveness of this therapy has only recently developed and the LCDs have not yet caught up with recent developments.

Pursuant to 42 C.F.R. § 405.1062, ALJs are not bound by LCDs, but will give substantial deference to these policies if they are applicable to a particular case. Furthermore, if an ALJ declines to follow a policy in a particular case, the ALJ must explain the reasons why the policy was not followed. *See* 42 C.F.R. § 405.1062. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect. *See id.*

Given the lack of information provided by L34823 – and that there is no NCD on this topic – this Judge declines to follow L34823 in this particular case because this Judge finds that the therapy in question has been proven to be safe and effective and is medically reasonable and necessary to treat REDACTED’s condition. This Judge explains his rationale as follows:

Optune (TTFields therapy) Has Been Proven Safe and Effective Based on Authoritative Evidence

Because there is no NCD and the LCD lacks any details or guidelines, this Judge must decide whether Optune (TTFields therapy) has been proven safe and effective based on authoritative evidence. MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110; *see also Almy*, 679 F.3d at 299. Such decisions should be based on either “published authoritative evidence” such as “definitive randomized clinical trials” or “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

Based on the hearing testimony; medical evidence and studies submitted; and FDA approval of the device, this Judge finds that the therapy in question has been proven safe and effective based on authoritative evidence.

First, this Judge takes into account Dr. [REDACTED]'s hearing testimony. Dr. [REDACTED] is board certified in internal medicine and medical oncology. (Hearing CD.) He testified that he has been treating brain tumors for thirty years. (*Id.*) Dr. [REDACTED] stated that recurrent glioblastoma multiforme is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. (Ex. 3, pg. 5; Hearing CD.) He testified that recent clinical studies of the effect of treating GBM patients with TTFields therapy with Temozolomide have shown significant improvements – approximately 50% – in survival rates. (*Id.*) He stated that the safety and efficacy of TTFields therapy is generally accepted in the medical community. (*Id.*)

Furthermore, Mr. Dan McCoy, [REDACTED] representative who is affiliated with NovoCure, testified that the Health Plan has paid for this therapy for GBM patients in the past. (Hearing CD.) He also testified that there are approximately 230 treatment sites in the country with physicians who are certified to prescribe the therapy in question. (*Id.*)

Second, in addition to studies on TTFields therapy included in the medical record, the Appellant submitted as new evidence results from a phase 3 clinical trial comparing Optune in combination with temozolomide to temozolomide alone in 700 patients with newly diagnosed GBM.³ (Ex. 6, pp. 17-27.)

This Judge may consider new evidence if there is “good cause” for the party to submit the evidence for the first time at this level of review. 42 C.F.R. § 405.1028. This Judge finds that “good cause” exists because the results of this study were only recently released and are very relevant to the issue at hand.

The objective of this study was to evaluate the efficacy and safety of TTFields used in combination with temozolomide maintenance treatment after chemoradiation therapy for patients with glioblastoma. (Ex. 6, pp. 17-27.) The results of this study essentially proved that in 315 patients with glioblastoma who had completed standard chemoradiation therapy, adding TTFields to maintenance temozolomide chemotherapy significantly prolonged progression-free and overall survival. (*Id.*)

After a thorough review of the clinical studies, this Judge finds the studies creditable in establishing the efficacy of TTFields therapy in prolonging and improving the survival of patients diagnosed with GBM.

Finally, this Judge finds that the Optune device is FDA approved, which is further evidence that it is “safe” and “effective.” (Ex. 3, pp. 110-14.) Medicare law states that FDA clearance is *necessary*, but not *sufficient*, for Medicare coverage. *Int’l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002. Specifically, FDA review seeks to determine whether a device is “safe and effective” such

³ Stupp R, Taillibert S, Kanner AA, et al. Maintenance Therapy With Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma: A Randomized Clinical Trial. *JAMA*. 2015;314(23):2535-2543. doi:10.1001/jama.2015.16669. See <http://jama.jamanetwork.com/article.aspx?articleid=2475463>

that it can be marketed to the general public. By contrast, Medicare coverage review seeks to determine whether the device is “reasonable and necessary” for treatment such that the device is worth the government’s money. MBPM, ch. 15, § 110.1; *Int’l Rehabilitative Scis. Inc.*, 688 F.3d at 1002. Therefore, this Judge finds FDA approval to be further evidence of Optune’s safety and effectiveness, but does not find FDA approval to be evidence of the reasonableness and necessity of the therapy for REDACTED

Optune (TTFields Therapy) is Medically Reasonable and Necessary to Treat REDACTED Condition

This Judge finds Optune (TTFields therapy) to be medically reasonable and necessary for REDACTED because it is an appropriate treatment of REDACTED condition and there is no medically appropriate and realistically feasible alternative pattern of care for REDACTED MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110.

First, this Judge takes into account the medical record and hearing testimony. The medical record and hearing testimony prove that REDACTED is a RED year old gentleman who is diagnosed with GBM. REDACTED presented with speech difficulty in July of 2015. (Ex. 3, pp. 2-3; Hearing CD.) An MRI revealed a mass in the left lateral temporal lobe. (*Id.*) On August 10, 2015, he underwent a craniotomy with pathology confirming GBM. (*Id.*) Dr. RED testified that during the surgery he was able to remove most of the tumor. (*Id.*) Dr. RED testified that following surgery, most patients relapse, and therefore they are started on radiation therapy with concurrent chemotherapy medication called Temozolomide. (*Id.*) REDACTED received five weeks of radiation therapy and is currently taking Temozolomide. (*Id.*)

Dr. RED stated that REDACTED has failed systemic surgery, chemotherapy and all radiotherapy options approved for this clinical scenario. (*Id.*) Therefore, he certified that “there are few if any available options that would benefit the patient in this clinical scenario.” (*Id.*) He certified that “Optune is currently the only chronic treatment option for recurrent glioblastoma that has established its survival benefit and safety profile in a randomized controlled trial against a control arm receiving active effective therapy.” (*Id.*)

This Judge also takes into account the FDA approval letter, which sets forth specific criteria for beneficiaries who would be considered candidates for TTFields therapy delivered by Optune:

This device is indicated for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically – or radiologically – confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy⁴, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 3, pg. 110.)

This Judge finds that REDACTED meets all the criteria set forth by the FDA.

⁴ This Judge notes that since this FDA approval letter dated April 8, 2011, the FDA has approved Optune in combination with temozolomide for the treatment of adult patients with newly diagnosed GBM. See http://www.abta.org/about-us/news/brain-tumor-news/fda-approves-optune-in_oct15.html

Based on the foregoing evidence, this Judge finds that Optune (TTFields therapy) has been proven to be safe and effective and is medically reasonable and necessary to treat REDACTED's condition.

Conclusions of Law


This Judge concludes that the Health Plan is **required** to pre-approve coverage of Optune (TTFields therapy) (CPT code E0766) for treatment of REDACTED glioblastoma pursuant to Medicare Part C provisions of Title XVIII of the Social Security Act and the terms of the Health Plan.

Order

The parties are DIRECTED to comply with this decision.

SO ORDERED.

Dated: DEC 22 2015



Roger Davis
U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri**

Appeal of: [REDACTED]	ALJ Appeal No.: 1-7512903660
Beneficiary: [REDACTED]	Medicare Part: C TexanPlus Classic HMO
HICN: *****4176A	Before: Roger Davis U.S. Administrative Law Judge

DECISION

This Judge decides this appeal **fully favorable** for [REDACTED] (the “Appellant”) after holding a telephonic hearing.

Findings of Fact

The Appellant seeks pre-approval of tumor treatment field therapy (E0766) for treatment of progressive glioblastoma multiform (GBM)¹. The Novo TFF-100A device is manufactured by Novocure (also referred to as Optune) and is relatively new to cancer treatment. This non-invasive treatment system is used in the beneficiary’s home, and delivers tumor treating fields therapy (TTF) to the brain to disrupt rapid cell division exhibited by recurrent GBM tumors. The system is comprised of a durable electrical field generator and disposable insulated transducer arrays (worn affixed to the scalp) for use with the portable generator. The system also includes lithium ion batteries, battery rack, battery charger, power supply, connection cables, and a carrying case. The device is indicated for treatment of adult patients with histologically-confirmed glioblastoma multiforme, following histologically or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (See Ex. 6; Ex. 3; and Hearing CD).

¹ On January 1, 2014, CMS created a new code, E0766, to group all billing, including all components/supplies and monthly rental fees, for NovoTTF-100A. Prior to this new code, the Appellant used multiple miscellaneous codes to bill the items, including: A9999, A9900, E1399, and A4555. This Judge takes note of the different codes used to bill the device, but does not purport to dictate how or under which code payment should be affected and/or authorized. The legal analysis will address whether coverage is supported by the documentation submitted.

This device was approved by the Federal and Drug Administration (FDA) in April of 2011. The device was approved after the pre-market approval pathway (PMA). This is the most rigorous medical device approval pathway, and is analogous to the FDA new drug pathway. The FDA approved the device on the basis of a multi-center randomized controlled pivotal (phase III) clinical trial. This was then followed by a positive vote from the FDA's independent Medical Device Advisory Committee's Neurological Devices Panel. The device falls within the DME benefit category according to a July 26, 2013 letter from CMS. In October 2015, this approval was extended to patients with newly diagnosed GBM in combination with temozolomide. (Ex. 6, p. 12). The device is also included in the National Comprehensive Cancer Network Guidelines ("NCCN Guidelines") as the standard of care for recurrent glioblastoma; as well as category one for newly diagnosed. The NCCN Guidelines are not binding in making Medicare coverage decisions.

The Enrollee is a 65-year-old female diagnosed with recurrent glioblastoma multiforme progressive. (Ex. 3, pp. 2-54, 19). Glioblastomas (GBM) are tumors that arise from astrocytes—the star-shaped cells that make up the “glue-like,” or supportive tissue of the brain. These tumors are usually highly malignant because the cells reproduce quickly and they are supported by a large network of blood vessels. (See <http://www.abta.org/brain-tumor-information/types-of-tumors/glioblastoma.html>). Recurrent glioblastoma multiforme progressive is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. There are few, if any, available options that would benefit the patient in this clinical scenario. Patients with recurrent GBM have a one-year survival rate of approximately 10% and a median overall survival time of three to five months when not treated with an effective (active) therapy.

The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by radiation and chemotherapy using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

The records indicate the Enrollee's glioblastoma was recurrent, progressive, stage IV, and supratentorial in location. (Ex. 3, pp. 1-4, 19; and Hearing CD). The Enrollee began TTF treatment on December 14, 2016, following diagnosis of GBM in July 2016. (Ex. 3, pp. 2-4). The treating physician recommended beginning TTF treatment because the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (*Id.*).

The medical records indicate the Enrollee had two unsuccessful brain surgeries (July 21, 2016 and April 28, 2017) in attempt to reduce tumor size. She had also undergone radiation and chemotherapy with both Temozolomide and Avastin. As of September 12, 2016 (four days short of the full initial chemo cycle), she was unable to continue Temozolomide because of low blood platelet counts. She continued Avastin, however. As of January 12, 2018, MRI impressions

showed stable appearance of the known GBM in the right dorsal thalamus, right dorsal midbrain, and posterior right mesial temporal lobe. (Ex. 3, pp. 1-3). The medical records specifically address the Enrollee's tumor progression – she was on both Avastin and TTF, so it had not progressed quickly, as she was sixteen months since diagnosis in July 2016. (Ex. 3, p. 4).

The Appellant testified they are relying on the newly diagnosed GBM FDA approval for TTF treatment, from December 14, 2016 until April 28, 2017. (Hearing CD).

Procedural History

The Part C Plan denied pre-approval for coverage of the medical equipment the provider sought. Then the Qualified Independent Contractor issued an unfavorable decision on the Appellant's appeal. Finally, the Appellant filed a request for a hearing before an Administrative Law Judge ("ALJ" or "Judge") with the Office of Medicare Hearings and Appeals ("OMHA").

This Judge conducted a hearing with representatives of the Appellant and the Plan on July 25, 2018. All evidence was admitted, and accordingly, the administrative record is now closed.

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

Individuals or organizations dissatisfied with the reconsideration of an initial determination are entitled to hearings before the Secretary of the Department of Health and Human Services. There must be a sufficient amount in controversy at the time of the request for hearing, and the appellant must timely submit the request for hearing. (42 C.F.R. § 405.1014; Social Security Act ("the Act") § 1869(b)(1)(A)). The Secretary delegates OMHA to administer the nationwide hearings and appeals system, and the ALJs within OMHA issue the final decisions of the Secretary, unless later reviewed by the Medicare Appeals Council. (*See* 70 Fed. Reg. 36386, 36387 (June 23, 2005)).

The request for hearing is timely if the Appellant files within sixty days after they receive the QIC Reconsideration determination. (*See* 42 C.F.R. §405.1002(a)(1)).

For requests filed in calendar year 2018, the required minimum amount remaining in controversy for an ALJ hearing is \$160.00 (following application of any co-insurance or deductible). (42 C.F.R. § 405.1006(b)(1)).

B. Scope of Review

The issues before the ALJ include any issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. (42 C.F.R. § 405.1000; 405.1032).

C. Standard of Review

The ALJ conducts a *de novo* review and issues a decision based on the hearing record. (42 § C.F.R. § 405.1000(d)). *De novo* review requires the ALJ to evaluate the record and controlling laws and render an independent assessment without regard to prior determinations and findings on the claim. All laws and regulations pertaining to Medicare are binding on ALJs, including but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations.

The Appellant bears the burden of proving each element of a Medicare claim by a preponderance of the evidence. Appellants must submit sufficient evidence in accordance with Medicare rules. (See §§1814(a)(1), 1815(b), and 1833(e) of the Act; 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, 405.1030).

I. Principles of Law

A. The Social Security Act and Regulations

Section 1862(a)(1) of the Social Security Act excludes Medicare payment for services which "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

Section 1832(a) of the Act states, in pertinent part: The benefits provided to an individual by the insurance program established by this Part shall entitle enrollees to have payment made to them or on their behalf for medical or other health services, subject to Medicare guidelines.

Section 1852 of the Act states that under Medicare Part C, a Medicare Advantage Organization offering a Medicare Advantage ("MA") plan must provide enrollees with coverage of those items and services for which benefits are available under Parts A and B. The Regulations support this basic requirement in 42 C.F.R. § 422.100(c), where it states: "An M+C plan includes at a minimum basic benefits, and also may include mandatory and optional supplemental benefits." Section 422.100(c)(1) defines basic benefits as ". . . all Medicare-covered services, except hospice services, and additional benefits as defined in § 422.2 and meeting all requirements in § 422.312." Each M+C organization must "[p]rovide coverage of, by furnishing, arranging for, or making payment for, all services that are covered by Part A and Part B of Medicare (if the enrollee is entitled to benefits under both parts) or by Medicare Part B (if entitled only under Part B) and that are available to beneficiaries residing in the plan's service area." (42 C.F.R. § 422.101(a)). An M+C organization plan may specify the networks of providers from whom enrollees may obtain services if the M+C organization ensures that all covered services are available and accessible under the plan. (42 C.F.R. § 422.112(a)).

The Regulations also provide for coverage for out of network services under circumstances where urgently needed services are necessary. (42 C.F.R. § 422.113(b)(iii)). Specifically, § 422.113(b)(iii) provides that *urgently needed services* means covered services that are not emergency services. Urgently needed services are provided when an enrollee is temporarily absent from the M+C plan's service (or, if applicable, continuation) area (or, under unusual and

extraordinary circumstances, provided when the enrollee is in the service or continuation area but the organization's provider network is temporarily unavailable or inaccessible) when the services are medically necessary and immediately required. The M+C organization is financially responsible for emergency and urgently needed services, regardless of whether the services are obtained within or outside the M+C organization, or if there is prior authorization for the services. (*See also CMS Medicare Managed Care Manual (Internet-Only Manual Pub. 100-16)* Ch. 4, Benefits and Beneficiary Protections, § 130.2 – Access and Availability Rules for Coordinated Care Plans).

Also, regulation 42 C.F.R. § 422.112 requires Medicare Advantage Organizations to provide or arrange for necessary specialty care. The Medicare Advantage Organization must arrange for specialty care outside of the plan provider network when network providers are not available or not adequate to meet an enrollee's medical needs.

Section 1833(e) of the Act states that no payment shall be made to any provider of services or other person under this Part unless the provider submits information that shows the amounts the provider is due for the periods at issue. (42 U.S.C. § 13951(e)).

The Medicare program, Title XVIII of the Social Security Act ("the Act"), is administered through the Centers for Medicare and Medicaid Services ("CMS"), a component of the United States Department of Health and Human Services ("HHS"). Under the authority of Section 1842(a) (1) (a) of the Act, the Secretary of HHS is authorized to enter into contracts with private entities for the day to day operations of the program. The designated contractor for the services at issue in this case is MAXIMUS Federal Services.

B. Medicare Part C

Section 1852 of the Act states that under Medicare Part C, a Medicare Advantage Organization offering an MA plan must provide enrollees with coverage of those items and services for which benefits are available under parts A and B. The Regulations support this basic requirement in 42 C.F.R. § 422.100(c), where it states, "An M+C plan includes at a minimum basic benefits, and also may include mandatory and optional supplemental benefits." Part (c)(1) defines basic benefits as "all Medicare-covered services..." While covering basic benefits, MA Organizations must, "provide coverage of, by furnishing, arranging for, or making payment for, all services that are covered by Part A and Part B of Medicare (if the enrollee is entitled to benefits under both parts) or by Medicare Part B (if entitled only under Part B) and that are available to beneficiaries residing in the plan's service area..."

While enrolled in a MA plan, an enrollee is entitled to and restricted by the limitations and conditions of that program with respect to Medicare coverage and reimbursement. In turn, the MA plan must make available to an enrollee, or provide reimbursement for, at least all services covered under Part A and Part B of Medicare. (42 C.F.R. § 422.101).

The Regulations also describe the authorities with which MA Organizations must comply while providing basic Part A and Part B services. The Regulation at 42 C.F.R. § 422.101(b) requires MA Organizations to comply with: (1) CMS's national coverage determinations; (2) general coverage guidelines included in original Medicare manuals and instructions unless superseded by operational policy letters or regulations in this part; and (3) written coverage decisions of local carriers and intermediaries with jurisdiction for claims in the geographic area in which services are covered under the M+C organization.

D. Statutes and Regulations

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services (CMS). Section 1831 of the Act establishes the Supplemental Medical Insurance Program for the aged and disabled under Part B.

Section 1832 of the Act establishes the scope of benefits provided to beneficiaries under the Medicare Part B insurance program. Under Section 1832(a)(2)(B) of the Act, an individual is entitled to payment for medical and other health services furnished by a provider of services, or by others as arranged by the provider of services. (*See also* 42 C.F.R. §410.3). No payment shall be made to any provider under the Act unless the provider furnishes information to determine the amounts due to them for the period at issue. (*See* 42 C.F.R. § 424.5(a)(6); and Title XVIII, § 1833(e) of the Act).

Medicare will pay for services that are reasonable and medically necessary for the diagnosis or treatment of a condition, illness, or injury to the beneficiary, or to improve the functioning of a malformed body member. (42 USC § 1395d(a)(1)). The provider must provide sufficient documentation to support the claim for payment. (42 C.F.R. § 424.5 (a)(6)).

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. Although not subject to the force and effect of law, CMS and its contractors have issued policy and guidelines describing the coverage criteria for selected types of medical services and supplies.

42 CFR Section 414.202 and the Chapter 15, Section 110.1 of the Medicare Benefit Policy Manual (CMS Publ. 100-2) provides, in relevant part, that durable medical equipment (“DME”) means equipment, furnished by a supplier or home health agency that –

- 1) Can withstand repeated use;
- 2) Is primarily and customarily used to serve a medical purpose;
- 3) Generally is not useful to an individual in the absence of an illness or injury; and
- 4) Is appropriate for use in the home.

Section 1879(a)(1) of Title XVIII of the Social Security Act provides in pertinent part, that when Medicare coverage is precluded under Section 1862(a)(1)(A) of the Act, i.e. the billed services were not reasonable and necessary, payment will be made, despite the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably been expected to know that the item was not covered. This is the limitation of liability provision. In other words, if either the beneficiary or the provider knew or had reason to know the service would not be covered, they are responsible for payment.

E. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (“LMRPs”) or local coverage determinations (“LCDs”).

As of the date of diagnosis, the applicable Local Coverage Determination, L34823, stated that tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. (CGS Admin., Local Coverage Determination L34823: Tumor Treatment Field Therapy (TTFT)(LCD L34823)(July 2016)).

Medically Reasonable and Necessary Medical Services

Part B of the Medicare Act extends coverage to certain types of durable medical equipment (DME) for qualified recipients. 42 U.S.C. § 1395k(a); *id.* § 1395x(s)(6). Not all DME is guaranteed coverage under Medicare Part B, however. The Medicare statute explicitly provides that “no payment may be made under ... Part B of this subchapter for any expenses incurred for items ... [which] are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *Id.* § 1395y(a)(1)(A); *see also Almy v. Sebelius*, 679 F.3d 297, 299 (4th Cir. 2012).

Medicare coverage of DME is determined in one of three ways. First, Medicare issues a “national coverage determination” (NCD) binding throughout the Medicare system and not subject to review by administrative law judges. *Id.* § 1395ff(f)(1)(B). Second, one of the private insurance carriers with whom Medicare contracts to administer claims under Part B can issue a “local coverage determination” (LCD) “respecting whether or not a particular item or service is covered on an intermediary – or carrier-wide basis.” *Id.* § 1395ff(f)(2)(B); *see also Almy*, 679 F.3d at 299. Finally, if no NCD or LCD is in place, “contractors may make individual claim determinations,” including whether a particular DME meets the statutory requirement of being “reasonable and necessary.” 68 Fed. Reg. 63, 693.

Medicare also has developed guidance in the Medicare Program Integrity Manual (CMS Pub. 100-08) (MPIM), Ch. 13 at § 13.5.1, and the Medicare Benefit Policy Manual (CMS

Pub. 100-02) (MBPM), Ch. 15 at § 110 for Medicare contractors applying the “reasonable and necessary” standard.² A device is not “reasonable and necessary” – and thus is not eligible for Medicare coverage – if it is:

- Not “safe” and “effective” – that is, if the device has not “been proven safe and effective based on authoritative evidence” or is not “generally accepted in the medical community as safe and effective for the condition for which it is used”;
- “[E]xperimental” – that is, “investigational”;
- Not “[a]ppropriate” for the individual beneficiary’s needs; or
- “[S]ubstantially more costly than a medically appropriate and realistically feasible alternative pattern of care.”

See also Almy, 679 F.3d at 299; *Int’l Rehabilitative Scis. Inc. v. Sebelius*, 688 F. 3d 994, 997 (9th Cir. 2012).

The burden is on the claimant to show that the device is reasonable and necessary. *Almy*, 679 F.3d at 305.

Medicare also instructs contractors as to the type of evidence to be used in making these technical determinations. Such decisions should be based on either “published authoritative evidence” such as “definitive randomized clinical trials” or “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

Statement of the Issues

Whether the Plan should have approved the service or durable medical equipment?

Analysis

The crux of the issue in this appeal is whether the record establishes that the medical device at issue was medically reasonable and necessary for treatment of the beneficiary’s condition. The Qualified Independent Contractor (QIC) denied coverage for the medical equipment, reasoning that the device was not medically reasonable and necessary. (Ex. 1, pp. 3-6).

This Judge is aware that there is an LCD, specifically (CGS Admin., Local Coverage Determination L34823: Tumor Treatment Field Therapy (TTFT)(LCD L34823)(July 2016)). However, the LCD only summarily denies coverage stating that the device was not reasonable and necessary. This Judge also has reviewed three other LCD jurisdictions in search of further information and guidance; however, they provide no additional substantive information explaining the reason coverage is to be denied. This Judge speculates that the LCDs lack details

² ALJs and the Medicare Appeals Council are not bound by CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. 42 C.F.R. § 405.1062(a).

because the scientific evidence of the effectiveness of this therapy has only recently developed and the LCDs have not yet caught up with recent developments.

Pursuant to 42 C.F.R. § 405.1062, ALJs are not bound by LCDs, but will give substantial deference to these policies if they are applicable to a particular case. Furthermore, if an ALJ declines to follow a policy in a particular case, the ALJ must explain the reasons why the policy was not followed. *See* 42 C.F.R. § 405.1062. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect. *See id.* Accordingly, the reasons set forth below are intended to explain this Judge's deviation from the LCD discussed *supra*.

This Judge finds that the therapy in question has been proven to be safe and effective and is medically reasonable and necessary to treat this particular beneficiary's condition. This Judge explains the rationale as follows:

TTF Therapy Has Been Proven Safe and Effective Based on Authoritative Evidence

To determine whether coverage is appropriate, this Judge must decide whether TTF has been proven safe and effective based on authoritative evidence. (MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110; *see also Almy*, 679 F.3d at 299). Such decisions should be based on either "published authoritative evidence" such as "definitive randomized clinical trials" or "general acceptance by the medical community," with the caveat that "[a]cceptance by individual health care providers" and "limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community." MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

Based on the hearing testimony; medical evidence and studies submitted; NCCN Guidelines; and FDA approval of the device, this Judge finds that the device in question has been proven safe and effective based on authoritative evidence.

The record supports that recurrent glioblastoma multiforme is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. Recent clinical studies of the effect of treating GBM patients with TTF therapy with Temozolomide have shown significant improvements – approximately 50% – in survival rates. The safety and efficacy of TTF therapy is generally accepted in the medical community. After a thorough review of the clinical studies, this Judge finds the studies creditable in establishing the efficacy of TTF therapy in prolonging and improving the survival of patients diagnosed with GBM.

Finally, this Judge finds that the device is FDA approved, which is further evidence that it is "safe" and "effective." Medicare law states that FDA clearance is *necessary*, but not *sufficient*, for Medicare coverage. (*Int'l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Specifically, FDA review seeks to determine whether a device is "safe and effective" such that it can be marketed to the general public. By contrast, Medicare coverage review seeks to determine whether the device is "reasonable and necessary" for treatment such that the device is worth the government's money. (MBPM, ch. 15, § 110.1; *Int'l Rehabilitative Scis. Inc.*, 688 F. 3d at

1002). Therefore, this Judge finds FDA approval to be further evidence of the device's safety and effectiveness.

TTF Therapy is Medically Reasonable and Necessary to Treat this Particular Patient's Condition

This Judge finds the TTF therapy device at issue to be medically reasonable and necessary for the Enrollee because it is an appropriate treatment of the Enrollee's condition and since there is no medically appropriate and realistically feasible alternative pattern of care for the Enrollee. (MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110).

First, this Judge takes into account the medical record and hearing testimony. The standard of care for GBM includes the patient undergoing debulking surgery at diagnosis, if possible, followed by radiation and chemotherapy using temozolomide. Some patients have carmustine wafers implanted in the resection cavity at the time of surgery. This initial treatment is then followed by monthly courses of temozolomide which are repeated for six months or until disease progression. When the disease relapses (recurrent GBM) treatment options are limited. Only 20% of recurrent GBM patients are candidates for additional debulking surgery, with or without wafer placement at the time of recurrence. Most recurrent GBM patients in the U.S. are treated with Avastin (bevacizumab – a chemotherapy agent), or experimental treatments. Avastin is the only chemotherapy FDA-approved for treatment of recurrent GBM.

This Judge also takes into account the FDA approval letter, which sets forth specific criteria for beneficiaries who would be considered candidates for TTF therapy delivered by the Appellant:

This device is indicated for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically – or radiologically – confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy³, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted. (Ex. 2, pp. 4-8.)

Notably, in October 2015, this approval was extended to patients with newly diagnosed GBM in combination with temozolomide. (Ex. 6, p. 12; *see* Footnote 3 below; and Hearing CD).

The records indicate the Enrollee had the requisite diagnosis – glioblastoma multiforme. (Ex. 3; and Hearing CD). The records indicate the Enrollee's glioblastoma was recurrent, progressive, stage IV, and supratentorial in location. (Ex. 3, pp. 1-4, 19; and Hearing CD). The Enrollee began TTF treatment on December 14, 2016, following diagnosis of GBM in July 2016. (Ex. 3, pp. 2-4). The treating physician recommended beginning TTF treatment because the chemotherapy and radiation combination had to date been unsuccessful in reducing the tumor. (*Id.*).

³ This Judge notes that since this FDA approval letter dated April 8, 2011, the FDA has approved the Appellant's device* in combination with temozolomide for the treatment of adult patients with newly diagnosed GBM. *See* http://www.abta.org/about-us/news/brain-tumor-news/fda-approves-optune-in_oct15.html

The medical records indicate the Enrollee had two unsuccessful brain surgeries (July 21, 2016 and April 28, 2017) in attempt to reduce tumor size. She had also undergone radiation and chemotherapy with both Temozolomide and Avastin. As of September 12, 2016 (four days short of the full initial chemo cycle), she was unable to continue Temozolomide because of low blood platelet counts. She continued Avastin, however. As of January 12, 2018, MRI impressions showed stable appearance of the known GBM in the right dorsal thalamus, right dorsal midbrain, and posterior right mesial temporal lobe. (Ex. 3, pp. 1-3). The medical records specifically address the Enrollee's tumor progression – she was on both Avastin and TTF, so it had not progressed quickly, as she was sixteen months since diagnosis in July 2016. (Ex. 3, p. 4).

The Appellant testified they are relying on the newly diagnosed GBM FDA approval for TTF treatment, from December 14, 2016 until April 28, 2017. (Hearing CD). Accordingly, this Judge finds that the beneficiary meets all the criteria set forth by the FDA and the NCCN Guidelines.

Based on the foregoing evidence, this Judge finds that the TTF therapy device at issue has been proven to be safe and effective and is medically reasonable and necessary to treat the Enrollee's condition.

Conclusions of Law

Based upon the written evidence in the record and the testimony offered at the hearing, this Judge issues a **fully favorable** determination for [REDACTED] and concludes that **pre-approval and/or coverage is appropriate** for the NovoTTF-100A HCPCS code E0766. Coverage is supported by sufficient information as required by Sections 1862(a) and 1833(e) of the Social Security Act.

Order

The Medicare contractor is **DIRECTED** to process the claim in accordance with this decision.

AUG 03 2018

SO ORDERED.

Dated: _____


 Roger Davis
 U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri**

Appeal of:	ALJ Appeal No.: 1-7599412754
Beneficiary	Medicare Part C
HICN:	Before: Roger Davis U.S. Administrative Law Judge

DECISION

This Judge decides this appeal **fully favorable** to [the beneficiary and “Appellant”) after holding a telephonic hearing.

Findings of Fact

The beneficiary and Appellant, Ms. [redacted] was enrolled in a health plan that is offered by Priority Health (“the Health Plan”), a Medicare Advantage Organization (MAO). Ms. [redacted] sought coverage from the Health Plan for Optune tumor treatment field therapy (E0766) that she received from dates of service February 2, 2018 to June 11, 2018 for treatment of glioblastoma multiforme (GBM). (Ex. 1, pp. 25-26.) This device is relatively new to cancer treatment. This non-invasive system is used in the beneficiary’s home, and delivers tumor treating fields therapy (TTF) to the brain to disrupt rapid cell division exhibited by recurrent GBM tumors. The system is comprised of a durable electrical field generator and disposable insulated transducer arrays (worn affixed to the scalp) for use with the portable generator. The system also includes lithium ion batteries, battery rack, battery charger, power supply, connection cables, and a carrying case. (Ex. 3.)

Pursuant to new guidelines issued by the Food and Drug Administration (FDA) on October 5, 2015, the device is indicated for treatment of adult patients with histologically-confirmed glioblastoma multiforme. Specifically, Optune with temozolomide is indicated for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy.

Ms. [redacted] treating physician, Dr. [redacted] submitted a letter dated April 10, 2018 as follows:

is a 62 year old woman diagnosed with glioblastoma who had presented with a loss of consciousness or grand mal seizure. She had an MRI which revealed an abnormality in the right temporal parietal region. The MRI was repeated on April 14, 2017 and showed a 19x 19x 20 mm ring enhancing mass. Ms. then underwent a craniotomy. The pathology confirmed glioblastoma. She completed radiation therapy with concurrent Temodar in late 2017. After discussing treatment options with Ms. I decided to prescribe Optune in combination with temozolomide as this currently is the best option for treating her glioblastoma. (Ex. 1, pg. 25.)

Ms. passed away on June 15, 2018. (Hearing CD.)

Procedural History

Ms. sought coverage from the Health Plan for Optune tumor treatment field therapy (E0766) that she received from dates of service February 2, 2018 to June 11, 2018. (Ex. 1, pp. 25-26.) The Health Plan denied coverage for the services at issue. (Ex. 1, pp. 8-10.) The Medicare Part C Qualified Independent Contractor agreed with the Health Plan's decision that it did not have to cover the services in question. (Ex. 1, pp. 3-4.) Ms. then filed a request for a hearing before an Administrative Law Judge (ALJ) in the Office of Medicare Hearings and Appeals (OMHA).

This Judge conducted a telephonic hearing on August 15, 2018 with the following participants: Mr. Jorge Morales (appointed representative of Ms. Christine Valle (representative of Health Plan); Ms. Amy Morris (representative of the Health Plan); Dr. Kiran Devisetty (Ms. treating physician); Ms. Julie Miles (representative of Novocure); Mr. Dan McCoy (representative of Novocure); Ms. Stephanie Hales (attorney representing Novocure).

The record includes an Appointment of Representative Form dated August 30, 2017 in which the beneficiary assigned Mr. Jorge Morales and Novocure as her representatives. (Ex. 5, pg. 2.) Following the telephonic hearing, representatives for Novocure submitted a written Request for Substitution of Party following Ms. death on June 15, 2018. (Ex. 8, pp. 2-4.) Specifically, in this request, Mr. (Mrs. personal representative) named Mr. Dan McCoy and Ms. Julie Miles (representatives of Novocure) as substitute parties in this appeal before this Judge. (*Id.*) This Judge accepts and approves this request for substitution of party. All evidence was admitted, and accordingly, the administrative record is now closed.

During the telephonic hearing, representatives of the Health Plan made a motion for dismissal of the appeal due to death of the beneficiary. Pursuant to 42 C.F.R. § 405.1052(a)(4)(ii), this appeal is not subject to dismissal. Therefore, the motion to dismiss is denied and this Judge will proceed to decide this case on the merits.

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

Health Plan enrollees who are dissatisfied with their Health Plan because they did not receive healthcare to which they believe they were entitled to, or because they contest the cost of a service they received, are entitled to an appeal process. Social Security Act § 1852(g), 42 U.S.C. § 1395w-22(g), 42 C.F.R. §§ 422.560, 422.562. The appeal process includes, if necessary, a hearing before an ALJ. 42 C.F.R. § 422.562(b)(4). An ALJ within the Office of Medicare Hearing and Appeals shall perform a *de novo* review of the case provided that there is a sufficient amount in controversy and that the appellant files the appeal in a timely fashion. 42 U.S.C. § 1395ff(b)(1)(A); *see also* 42 C.F.R. §§ 422.600, 405.1000 and 405.1002. *See generally* 70 Fed. Reg. 36386, 36387 (June 23, 2005) (delegation of Secretary's power specifically to OMHA to conduct reviews).

The request for hearing is timely if the Appellant files within sixty days after they receive the QIC Reconsideration determination. (*See* 42 C.F.R. §405.1002(a)(1)).

For requests filed in calendar year 2018, the required minimum amount remaining in controversy for an ALJ hearing is \$160.00 (following application of any co-insurance or deductible). (42 C.F.R. § 405.1006(b)(1)).

B. Scope of Review

The issues before the ALJ include any issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. (42 C.F.R. § 405.1000; 405.1032).

C. Standard of Review

The ALJ conducts a *de novo* review and issues a decision based on the hearing record. (42 § C.F.R. § 405.1000(d)). *De novo* review requires the ALJ to evaluate the record and controlling laws and render an independent assessment without regard to prior determinations and findings on the claim. All laws and regulations pertaining to Medicare are binding on ALJs, including but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations.

The Appellant bears the burden of proving each element of a Medicare claim by a preponderance of the evidence. This is satisfied through the submission of sufficient evidence in accordance with Medicare rules. (*See* §§1814(a)(1), 1815(b), and 1833(e) of the Act; 42 C.F.R. §§ 424.5(a)(6), 405.1018, 405.1028, 405.1030).

II. Principles of Law

Managed Care Organizations

A managed care organization (MAO) offering a Medicare Advantage (MA) plan must provide enrollees with “basic benefits,” which are all items and services covered by Medicare Part A and Part B available to beneficiaries residing in the plan’s service area. 42 C.F.R. § 422.101(a). An MA plan “must provide enrollees in that plan with coverage of the basic benefits by furnishing the benefits directly or through arrangements, or by paying for the benefits.” 42 C.F.R. § 422.100(a). In providing “basic benefits,” an MAO must comply with national coverage determinations (NCDs) issued by CMS, “[g]eneral coverage guidelines included in original Medicare manuals and instructions unless superseded by operational policy letters or regulations in [part 422] or related instructions; and . . . [w]ritten coverage decisions of local Medicare contractors.” 42 C.F.R. § 422.101(b). At its discretion, an MA plan may also offer additional (or “supplemental”) benefits beyond those covered by original Medicare. 42 C.F.R. § 422.102.

Medically Reasonable and Necessary Medical Services

Part B of the Medicare Act extends coverage to certain types of durable medical equipment (DME) for qualified recipients. 42 U.S.C. § 1395k(a); *id.* § 1395x(s)(6). Not all DME is guaranteed coverage under Medicare Part B, however. The Medicare statute explicitly provides that “no payment may be made under . . . Part B of this subchapter for any expenses incurred for items . . . [which] are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *Id.* § 1395y(a)(1)(A); *see also Almy v. Sebelius*, 679 F.3d 297, 299 (4th Cir. 2012).

Medicare coverage of DME is determined in one of three ways. First, Medicare issues a “national coverage determination” (NCD) binding throughout the Medicare system and not subject to review by administrative law judges. *Id.* § 1395ff(f)(1)(B). Second, one of the private insurance carriers with whom Medicare contracts to administer claims under Part B can issue a “local coverage determination” (LCD) “respecting whether or not a particular item or service is covered on an intermediary – or carrier-wide basis.” *Id.* § 1395ff(f)(2)(B); *see also Almy*, 679 F.3d at 299. Finally, if no NCD or LCD is in place, “contractors may make individual claim determinations,” including whether a particular DME meets the statutory requirement of being “reasonable and necessary.” 68 Fed. Reg. 63, 693.

Medicare also has developed guidance in the Medicare Program Integrity Manual (CMS Pub. 100-08) (MPIM), Ch. 13 at § 13.5.1, and the Medicare Benefit Policy Manual (CMS Pub. 100-02) (MBPM), Ch. 15 at § 110 for Medicare contractors applying the “reasonable and necessary” standard.¹ A device is not “reasonable and necessary” – and thus is not eligible for Medicare coverage – if it is:

¹ ALJs and the Medicare Appeals Council are not bound by CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. 42 C.F.R. § 405.1062(a).

- Not “safe” and “effective” – that is, if the device has not “been proven safe and effective based on authoritative evidence” or is not “generally accepted in the medical community as safe and effective for the condition for which it is used”;
- “[E]xperimental” – that is, “investigational”;
- Not “[a]ppropriate” for the individual beneficiary’s needs; or
- “[S]ubstantially more costly than a medically appropriate and realistically feasible alternative pattern of care.”

See also Almy, 679 F.3d at 299; *Int’l Rehabilitative Scis. Inc. v. Sebelius*, 688 F. 3d 994, 997 (9th Cir. 2012).

The burden is on the claimant to show that the device is reasonable and necessary. *Almy*, 679 F.3d at 305.

Medicare also instructs contractors as to the type of evidence to be used in making these technical determinations. Such decisions should be based on either “published authoritative evidence” such as “definitive randomized clinical trials” or “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” MPIM § 13.7.1; *see also Almy*, 679 F.3d at 300.

Statement of the Issues

1. Whether the plan provisions have been met warranting payment or coverage?
2. Whether the plan should provide coverage for the services in question?

Analysis

The crux of the issue in this appeal is whether the record establishes that the medical device at issue was medically reasonable and necessary for treatment of the beneficiary’s condition. The Qualified Independent Contractor (QIC) denied coverage for the medical equipment stating that “Medicare rules for coverage of these services have not been met.” (Ex. 1, pg. 4.)

This Judge is aware that there is an LCD, specifically *NHIC Corp., Local Coverage Determination L34823: Tumor Treatment Field Therapy (LCD L34823) (Oct. 2015)*, which states that “tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.” However, the LCD only summarily denies coverage stating that the device was not reasonable and necessary. This Judge speculates that the LCDs lack details because the scientific evidence of the effectiveness of this therapy has only recently developed and the LCDs have not yet caught up with recent developments.

Pursuant to 42 C.F.R. § 405.1062, ALJs are not bound by LCDs, but will give substantial deference to these policies if they are applicable to a particular case. Furthermore, if an ALJ declines to follow a policy in a particular case, the ALJ must explain the reasons why the policy was not followed. *See* 42 C.F.R. § 405.1062. An ALJ decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect. *See id.*

This Judge finds that the therapy in question has been proven to be safe and effective and is medically reasonable and necessary to treat this particular beneficiary's condition. This Judge explains his rationale as follows:

TTF Therapy Has Been Proven Safe and Effective Based on Authoritative Evidence

Based on the hearing testimony; medical evidence and studies submitted; NCCN Guidelines; and FDA approval of the device, this Judge finds that the device in question has been proven safe and effective based on authoritative evidence.

The record supports that recurrent glioblastoma multiforme is considered by the National Institutes of Health as an orphan disease due to its rarity and lack of approved treatment options. Recent clinical studies of the effect of treating GBM patients with TTF therapy with Temozolomide have shown significant improvements – approximately 50% – in survival rates. The safety and efficacy of TTF therapy is generally accepted in the medical community. After a thorough review of the clinical studies, this Judge finds the studies creditable in establishing the efficacy of TTF therapy in prolonging and improving the survival of patients diagnosed with GBM.

Finally, this Judge finds that the device is FDA approved, which is further evidence that it is “safe” and “effective.” Medicare law states that FDA clearance is *necessary*, but not *sufficient*, for Medicare coverage. (*Int'l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Specifically, FDA review seeks to determine whether a device is “safe and effective” such that it can be marketed to the general public. By contrast, Medicare coverage review seeks to determine whether the device is “reasonable and necessary” for treatment such that the device is worth the government's money. (MBPM, ch. 15, § 110.1; *Int'l Rehabilitative Scis. Inc.*, 688 F. 3d at 1002). Therefore, this Judge finds FDA approval to be further evidence of the device's safety and effectiveness.

TTF Therapy is Medically Reasonable and Necessary to Treat this Particular Beneficiary's Condition

This Judge finds the TTF therapy device at issue to be medically reasonable and necessary for the beneficiary because it is an appropriate treatment of the beneficiary's condition and since there is no medically appropriate and realistically feasible alternative pattern of care for the beneficiary. (MPIM, Ch. 13 at § 13.5.1; MBPM, Ch. 15 at § 110).

First, this Judge takes into account the medical record and hearing testimony. Ms. Ross' treating physician, Dr. Kiran Devisetty, submitted a letter dated April 10, 2018 as follows:

is a 62 year old woman diagnosed with glioblastoma who had presented with a loss of consciousness or grand mal seizure. She had an MRI which revealed an abnormality in the right temporal parietal region. The MRI was repeated on April 14, 2017 and showed a 19x 19x 20 mm ring enhancing mass. Ms. then underwent a craniotomy. The pathology confirmed glioblastoma. She completed radiation therapy with concurrent Temodar in late 2017. After discussing treatment options with Ms. I decided to prescribe Optune in

combination with temozolomide as this currently is the best option for treating her glioblastoma. (Ex. 1, pg. 25.)

This Judge also takes into account new guidelines issued by the Food and Drug Administration (FDA) on October 5, 2015, which state that the device is indicated for treatment of adult patients with histologically-confirmed glioblastoma multiforme. Specifically, Optune with temozolomide is indicated for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy.

This Judge finds that the beneficiary meets all the criteria set forth by the FDA. (Hearing CD; Ex. 1, pg. 25; Ex. 4, pp. 4-7.) Specifically, the medical record shows that Ms. _____ suffered from newly diagnosed supratentorial glioblastoma. (*Id.*) She underwent craniotomy and completed radiation therapy with concurrent Temodar in late 2017. (*Id.*) She then was prescribed Optune in combination with temozolomide. (*Id.*)

Based on the foregoing evidence, this Judge finds that the TTF therapy device at issue has been proven to be safe and effective and is medically reasonable and necessary to treat the beneficiary's condition.

Conclusions of Law

This Judge decides this appeal **favorable** to the Appellant and concludes that the Health Plan is **required** to provide coverage for Optune tumor treatment field therapy (E0766) that Ms. _____ received from dates of service February 2, 2018 to June 11, 2018 for treatment of glioblastoma multiforme (GBM) pursuant to Medicare Part C provisions of Title XVIII of the Social Security Act and the terms of the Health Plan.

Order

The Medicare contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: SEP 07 2018


Roger Davis
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of:	OMHA Appeal No.: 1-7284583580
Enrollee:	Medicare: Part C
HICN: *****7632A	Before: Arthur DePrez Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is entered for the Appellant/Beneficiary.

Procedural History

Appellant/Beneficiary, is requesting that BCBS of Michigan Mutual Insurance Company (hereinafter referred to as "the Plan") provide her with pre-approval of Optune Device. After initial and reconsideration determinations, Maximus found that the Plan did not have to provide the beneficiary with pre-approval of Optune Device. The Appellant/Beneficiary timely requested a hearing before an Administrative Law Judge, seeking provision of the item at issue. The amount in controversy satisfies the jurisdictional requirement for a hearing (§1869(E) of the Social Security Act; 67 Fed. Reg. 62478 and 42 C.F.R. §405.1006).

A telephone hearing was held on March 14, 2018 at 9:30AM. The relevant parties received a valid notice of hearing and/or were present for the duly scheduled hearing.

Issues

Whether the Appellant/Beneficiary is entitled to the pre-approval of Optune Device.

Findings of Fact

1. The amount in controversy satisfies the jurisdictional requirement for an Administrative Law Judge decision.

2. The Appellant/Beneficiary, timely filed a request for an Administrative Law Judge hearing.
3. The Plan's does not provide coverage of the Optune Device.
4. Under Traditional Medicare there is a local coverage determination that Optune Device shall be denied as non-covered.
5. The undersigned is required to give substantial deference to local coverage determinations but is not bound by them.
6. In this instance there is cause to divert from the local coverage determination, not because it is faulty but because of the facts of this specific case support payment under traditional Medicare.
7. Since the facts support payment under Traditional Medicare and the Plan is following Traditional Medicare rules for this service the Plan is required to cover the Optune Device.
8. The Appellant/Beneficiary entitled to pre-approval of Optune Device as it is should be covered by Traditional Medicare in this instance.

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of HHS, provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. See 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJ's within OMHA issue the final decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.* For requests filed in calendar year 2010, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible). See §1869(b)(1)(E) of the Act, 74 Fed. Reg. 48976 (Sept. 2, 2009). See also 42 C.F.R. § 405.1006(b), 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing, if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing, or, if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a de novo review of each claim at issue and issues a decision based on the hearing record. 42 C.F.R. 405.1000(d) and Section 557 of the Administrative Procedure Act. A de novo review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. All laws and regulations pertaining to the Medicare and Medicaid programs, including, but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations, are binding on ALJ's. 42 C.F.R. § 405.1063. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). See e.g., Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; see also 42 C.F.R. § 424.5(a)(6), 42 C.F.R. § 405.1018, 42 C.F.R. § 405.1028, and 42 C.F.R. § 405.1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into the record. *Id.*

II. Principles of Law

A. Statutes and Regulations

Title XVIII of the Social Security Act §1862(a)(1) of states the items and services that are reasonable and necessary for the diagnosis and treatment of illness or injury that are covered under the Medicare Program.

Title XVIII of the Social Security Act §1833(e) states in pertinent part herein: no payment shall be made to any provider of services or other person under this part unless there has been furnished such information as may be necessary in order to determine the amounts due such provider or other person under this part for the period with respect to which the amounts are being paid or for any prior period.

Title XVIII of the Social Security Act, §1879

a) Where—

(1) a determination is made that, by reason of section 1862(a)(1) or (9) or by reason of a coverage denial described in subsection (g), payment may not be made under part A or part B of this title for any expenses incurred for items or services furnished an individual by a provider of services or by another person pursuant to an assignment under section 1842(b)(3)(B)(ii), and

(2) both such individual and such provider of services or such other person, as the case may be, did not know, and could not reasonably have been expected to know, that payment would not be made for such items or services under such part A or part B,

then to the extent permitted by this title, payment shall, notwithstanding such determination, be made for such items or services (and for such period of time as the Secretary finds will carry out the objectives of this title), as though section 1862(a)(1) and section 1862(a)(9) did not apply and as though the coverage denial described in subsection (g) had not occurred.

Title XVIII of the Social Security Act, § 1851 (*in pertinent part*)

(a) CHOICE OF MEDICARE BENEFITS THROUGH MEDICARE+CHOICE PLANS.—

(1) IN GENERAL.—Subject to the provisions of this section, each Medicare+Choice eligible individual (as defined in paragraph (3)) is entitled to elect to receive benefits (other than qualified prescription drug benefits) under this title—

(A) through the original medicare fee-for-service program under parts A and B, or

(B) through enrollment in a Medicare+Choice plan under this part, and may elect qualified prescription drug coverage in accordance with section 1860D-1.

Title XVIII of the Social Security Act, § 1852 (*in pertinent part*)

(a) BASIC BENEFITS.—

Requirement.—

(1) IN GENERAL.—Except as provided in section 1859(b)(3) for MSA plans and except as provided in paragraph (6) for MA regional plans[129], each Medicare+Choice plan shall provide to members enrolled under this part, through providers and other persons that meet the applicable requirements of this title and part A of title XI, benefits under the original medicare fee-for-service program option (and, for plan years before 2006, additional benefits required under section 1854(f)(1)(A))

(B) BENEFITS UNDER THE ORIGINAL MEDICARE FEE-FOR-SERVICE PROGRAM OPTION DEFINED.—

(i) IN GENERAL.—For purposes of this part, the term “benefits under the original medicare fee-for-service program option” means those items and services (other than hospice care) for which benefits are available under parts A and B to individuals entitled to benefits under part A and enrolled under part B, with cost-sharing for those services as required under parts A and B or an actuarially equivalent level cost-sharing as determined in this part.

- (ii) **SPECIAL RULE FOR REGIONAL PLANS.**—In the case of an MA regional plan in determining an actuarially equivalent level of cost-sharing with respect to benefits under the original medicare fee-for-service program option, there shall only be taken into account, with respect to the application of section 1858(b)(2), such expenses only with respect to subparagraph (A) of such section.

(3) SUPPLEMENTAL BENEFITS.—

(A) BENEFITS INCLUDED SUBJECT TO SECRETARY'S APPROVAL.—

Each Medicare+Choice organization may provide to individuals enrolled under this part, other than under an MSA plan (without affording those individuals an option to decline the coverage), supplemental health care benefits that the Secretary may approve. The Secretary shall approve any such supplemental benefits unless the Secretary determines that including such supplemental benefits would substantially discourage enrollment by Medicare+Choice eligible individuals with the organization.

(B) AT ENROLLEES OPTION.—

- (i) **IN GENERAL.**—Subject to clause (ii), a Medicare+Choice organization may provide to individuals enrolled under this part supplemental health care benefits that the individuals may elect, at their option, to have covered.

- (ii) **SPECIAL RULE FOR MSA PLANS.**—A Medicare+Choice organization may not provide, under an MSA plan, supplemental health care benefits that cover the deductible described in section 1859(b)(2)(B). In applying the previous sentence, health benefits described in section 1882(u)(2)(B) shall not be treated as covering such deductible.

(C) APPLICATION TO MEDICARE+CHOICE PRIVATE FEE-FOR-SERVICE PLANS.—Nothing in this paragraph shall be construed as preventing a Medicare+Choice private fee-for-service plan from offering supplemental benefits that include payment for some or all of the balance billing amounts permitted consistent with section 1852(k) and coverage of additional services that the plan finds to be medically necessary.

42 CFR §422.100(c) states in pertinent part that Medicare Advantage plans must include basic benefits at a minimum and may also include mandatory and optional supplemental benefits. Basic benefits are defined as "all Medicare covered services, except hospice services." Mandatory supplemental benefits are defined as "services not covered by Medicare that an MA enrollee must purchase as part of an MA plan that are paid for in full, directly by (or on behalf of) Medicare enrollees, in the form of premiums or cost-sharing. Optional supplemental benefits are defined as "health services not covered by Medicare that are purchased at the option of the MA enrollee and paid for in full, directly by (or on behalf of) the Medicare enrollee, in the form of premiums or cost-sharing. These services may be grouped or offered individually."

42 CFR §422.101 states in pertinent part that Medicare Advantage Organization (MA) health plans must provide coverage for all services that are covered by Part A and Part B of Medicare (if the enrollee is entitled to benefits under both parts) or by Medicare

Part B (if entitled only under Part B)). Further, MA's must comply with national coverage determinations as promulgated by the Centers for Medicare and Medicaid Services.

42 CFR §405.1062 provides that Administrative Law Judges will give substantial deference to LCD's, LMRP's, or CMS program guidance when applicable and if they do not follow the policy they must explain why in their decision

B. Policy and Guidelines

Local Coverage Determination L34823, Tumor Treatment Field Therapy

Tumor Treatment Field Therapy Policy Article (A52711)

Analysis

This matter is before the Administrative Law Judge on the basis of an appeal filed by (hereinafter referred to as the Appellant/Beneficiary) on or about February 9, 2018. (Ex. 3). The Appellant/Beneficiary requested an Administrative Law Judge review of the denial of her request for pre-approval of Optune Device. Maximus denied the request stating as its rationale that: "Medicare does not considered this device to be medically reasonable or necessary, as it is considered tumor treatment field therapy. Based on this information, we decided that Medicare coverage rules for the coverage of the device have not been met. Therefore, we decided that BCBS does not have to pre-approve Optune Device.

The Appellant/Beneficiary's contention is that the device is FDA approved for patients newly diagnosed with Glioblastoma. In support of this position the Appellant/Beneficiary presented evidence in the form of documentation and sworn testimony. The evidence demonstrates that the Appellant/Beneficiary was diagnosed with left parietal glioblastoma for which the Optune device was prescribed. Per the FDA coverage guidelines this is the exact condition that the Optune device is intended to treat and the diagnosis for which it is approved. *Medical Devices; Availability of Safety and Effectiveness Summaries for Premarket Approval Applications*, 81 Fed. Reg. 6865 (Feb. 9, 2016).

The undersigned has reviewed the available evidence, the Plan's Evidence of Coverage and Traditional Medicare guidelines and finds that while ALJs are required to give substantial deference to Local Coverage Determinations, they are not bound by them. The applicable local coverage determination states that tumor treatment field therapy shall be denied as not reasonable and necessary in this specific instance the overall medical evidence demonstrates medical necessity for this item. The beneficiary is newly diagnosed with left parietal glioblastoma the exact condition for which the Optune device was approved by the FDA. *Id.* The medical records clearly show said new diagnosis and the treating physician testified to said diagnosis as well as the beneficiary's need for the device at issue.

Conclusions of Law

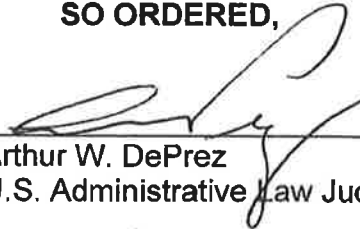
It is the decision of the undersigned Administrative Law Judge that the services in question requested by the Appellant/Beneficiary are covered by Traditional Medicare and therefore have to be covered under Medicare Part C.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED,

Dated: **APR 23 2018** _____



Arthur W. DePrez
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of:

REDACTED

OMHA Appeal No.: 1-7772250246

Beneficiary:

Medicare: **Part B**

Medicare No.:

Before: **Arthur DePrez**
Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is entered for the Appellant/Beneficiary REDACTED

Procedural History

REDACTED the Appellant, underwent Electrical Stimulation Cancer Treatments (E0766) via the Optune device on July 7, 2017, August 7, 2017, and September 7, 2017. After initial and reconsideration determinations, the QIC denied coverage for those dates of service. The Appellant/Beneficiary timely requested a hearing before an Administrative Law Judge, seeking coverage for all services provided on July 7, 2017, August 7, 2017, and September 7, 2017. The amount in controversy satisfies the jurisdictional requirement for a hearing (§1869(E) of the Social Security Act; 67 Fed. Reg. 62478 and 42 C.F.R. §405.1006).

A telephone hearing was held on October 17, 2018 at 10:30AM. The relevant parties received legally sufficient notice of said hearing and/or were present for said same hearing.

Issues

Whether the available evidence sufficiently establishes that the Electrical Stimulation Cancer Treatments (E0766) provided to the Appellant/Beneficiary on July 7, 2017, August 7, 2017, September 7, 2017 were covered by Medicare, medically necessary and properly documents and if not who is liable for the non-covered charges.

Findings of Fact

1. The amount in controversy satisfies the jurisdictional requirement for an Administrative Law Judge decision.
2. The Appellant, timely filed a request for an Administrative Law Judge hearing.
3. The Appellant/Beneficiary was diagnosed with glioblastoma in 2015 and prescribed surgery, radiation, chemotherapy and the Electrical Stimulation Cancer Treatments (E0766) via the Optune device.
4. The Appellant/Beneficiary underwent a resection on June 25, 2015 and has been presenting with speech difficulty including stuttering since May 5, 2015.
5. The medical record documents increasing memory problems, confusion, and unsteadiness prior to the item at issue being provided.
6. The Optune device is FDA approved, has been efficacious for the Appellant/Beneficiary and he continues to live.
7. The Optune device used to deliver Electrical Stimulation Cancer Treatments (E0766) was delivered to the Appellant/Beneficiary on April 7, 2017.
8. The Appellant/Beneficiary is entitled to Medicare reimbursement for the services in question with date of service of July 7, 2017, August 7, 2017, and September 7, 2017.

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of HHS, provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. See 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJ's within OMHA issue the final decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.* For requests filed in calendar year 2010, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible). See §1869(b)(1)(E) of the Act, 74 Fed.

Reg. 48976 (Sept. 2, 2009). See also 42 C.F.R. § 405.1006(b), 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing, if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing, or, if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a de novo review of each claim at issue and issues a decision based on the hearing record. 42 C.F.R. 405.1000(d) and Section 557 of the Administrative Procedure Act. A de novo review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. All laws and regulations pertaining to the Medicare and Medicaid programs, including, but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations, are binding on ALJ's. 42 C.F.R. § 405.1063. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). See e.g., Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; see also 42 C.F.R. § 424.5(a)(6), 42 C.F.R. § 405.1018, 42 C.F.R. § 405.1028, and 42 C.F.R. § 405.1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into the record. *Id.*

II. Principles of Law

A. Statutes and Regulations

Social Security Act §1862(a)(1) of states the items and services that are reasonable and necessary for the diagnosis and treatment of illness or injury that are covered under the Medicare Program.

Social Security Act §1833(e) states in pertinent part herein: no payment shall be made to any provider of services or other person under this part unless there has been furnished such information as may be necessary in order to determine the amounts

due such provider or other person under this part for the period with respect to which the amounts are being paid or for any prior period.

Social Security Act, §1879

a) Where—

(1) a determination is made that, by reason of section 1862(a)(1) or (9) or by reason of a coverage denial described in subsection (g), payment may not be made under part A or part B of this title for any expenses incurred for items or services furnished an individual by a provider of services or by another person pursuant to an assignment under section 1842(b)(3)(B)(ii), and

(2) both such individual and such provider of services or such other person, as the case may be, did not know, and could not reasonably have been expected to know, that payment would not be made for such items or services under such part A or part B,

then to the extent permitted by this title, payment shall, notwithstanding such determination, be made for such items or services (and for such period of time as the Secretary finds will carry out the objectives of this title), as though section 1862(a)(1) and section 1862(a)(9) did not apply and as though the coverage denial described in subsection (g) had not occurred.

42 CFR 424.5(a)(6) As a basis for Medicare payment, the following conditions must be met:

(6)Sufficient information. The provider, supplier, or beneficiary, as appropriate, must furnish to the intermediary or carrier sufficient information to determine whether payment is due and the amount of payment

42 CFR 405.1062 Applicability of local coverage determinations and other policies not binding on the ALJ or attorney adjudicator and Council.

(a) ALJs and attorney adjudicators and the Council are not bound by LCDs, LMRPs, or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case.

(b) If an ALJ or attorney adjudicator or Council declines to follow a policy in a particular case, the ALJ or attorney adjudicator or Council decision must explain the reasons why the policy was not followed. An ALJ or attorney adjudicator or Council decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect.

(c) An ALJ or attorney adjudicator or the Council may not set aside or review the validity of an LMRP or LCD for purposes of a claim appeal. An ALJ or the DAB may review or set aside an LCD (or any part of an LMRP that constitutes an LCD) in accordance with part 426 of this title.

B. Policy and Guidelines**Local Coverage Determination L34823****Analysis**

This matter is before the Administrative Law Judge on the basis of an appeal filed by M. REDACTED the Appellant/Beneficiary. The Appellant/Beneficiary is requesting a review of the QICs denial of the claim(s) for Electrical Stimulation Cancer Treatments (E0766). The denial rational employed by the QIC was: "In this instance, the medical documentation received indicates the beneficiary has a diagnosis of malignant neoplasm of the temporal lobe (C71.2). However, the medical documentation does not support the need for the device. There is insufficient documentation to quantify the effects of the device for this beneficiary. Based on the available documentation, the requirements of the DME MAC's LCD policy L34823 have not been met." (Exh. 1 p. 4).

The Appellant disagrees with this position and contends that: "This is the technology that clinicians treating central nervous system tumors have embraced. No basis exists to deny Medicare coverage of a device that is shown in the peer-reviewed literature to be a safe and effective treatment for glioblastoma, a life threatening condition. The Optune system was approved as safe and effective by the FDA. The peer-reviewed literature further supports its efficacy and the improved clinical outcome of patients who use the device. It is incorporated in the NCCN guidelines (considered the gold standard for cancer care), and it enjoys widespread adoption by clinicians and all the major payers in the United States based on the foregoing. The claim should be approved. Of particular note, if the QIC insists on quantifying the effectiveness of the treatment, Mr. REDACTED offers that his extended survival more than adequately demonstrates the effectiveness of this important device." (Exh. 4 p. 5). In support of this position the Appellant provided evidence in the form of documentation and sworn testimony. The evidence demonstrates that the Appellant/Beneficiary was diagnosed with glioblastoma in 2015 and prescribed surgery, radiation, chemotherapy and the Electrical Stimulation Cancer Treatments (E0766) via the Optune device; that he underwent a resection on June 25, 2015 and has been presenting with speech difficulty including stuttering since May 5, 2015; that he demonstrated increasing memory problems, confusion, and unsteadiness; that the Optune device is FDA approved, has been efficacious for the Appellant/Beneficiary and he continues to live and that the Optune device is being used to deliver Electrical Stimulation Cancer Treatments (E0766) and was delivered to the Appellant/Beneficiary on April 7, 2017. Additionally, patients diagnosed with glioblastoma typically have a one year survival of about 10% of patients as it is uniformly fatal the Appellant/Beneficiary is still living three years after diagnosis.

While, LCD L34823 indicates that E0766 treatment is not reasonable and necessary, the facts of this case demonstrate that this treatment is FDA approved, is efficacious for this patient and that he continues to live as a result of these treatments. The undersigned gave substantial deference to LCD L34823 however, after taking note of the Appellant/Beneficiary's limited treatment options, support for the use of this item/process based on clinical study outcomes/statements/policies, FDA approval and other payers' policies. The undersigned has reviewed the available evidence and finds that the

available evidence establishes the medical necessity of the Electrical Stimulation Cancer Treatments (E0766) due to the Appellant/Beneficiary's diagnosis of glioblastoma and that it is therefore payable by Medicare.

Since the Electrical Stimulation Cancer Treatments (E0766) provided on July 7, 2017, August 7, 2017, September 7, 2017 are covered, §1879 does not apply.

Conclusions of Law

The Electrical Stimulation Cancer Treatments (E0766) provided on July 7, 2017, August 7, 2017, September 7, 2017 were medically reasonable and necessary and a covered service under Medicare Part B. The provider is entitled to Medicare payment for that date.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED,

Dated: _____

NOV 27 2018



Arthur W. DePrez
U.S. Administrative Law Judge



U.S. Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of:	REDACTED	ALJ Appeal No.:	1-7919430214
Beneficiary:		Medicare Part:	B
HICN:	*****6747A	Before:	Arthur DePrez U.S. Administrative Law Judge

DECISION

After considering the evidence and arguments, a **FULLY FAVORABLE** decision is entered for REDACTED ("Appellant").
D

Procedural History

Appellant submitted a claim to Medicare for radiation services, billed under HCPCS code E0766, electrical stim cancer treatment provided to the beneficiary REDACTED on January 27, 2018, February 27, 2018 and March 27, 2018. (Ex. 1) Appellant's claims were denied by Noridian Healthcare Solutions, a Medicare Administrative Contractor (Contractor) at the initial and redetermination levels. The Appellant requested reconsideration, and on September 5, 2018, C2C Innovative Solutions, Inc., a Medicare Qualified Independent Contractor (QIC), denied the claim for the radiation services.

On October 1, 2018, the Appellant made a timely request for an Administrative Law Judge (ALJ) hearing before the Office of Medicare Hearings and Appeals (OMHA). 42 C.F.R. § 405.1014(b)(1). (*Id.*) The amount in controversy satisfies the jurisdictional requirement for a hearing decision as defined in §1869 (e) of Title XVIII of the Social Security Act (The Act).

On December 17, 2018, a telephonic hearing was held from the Office of Medicare Hearings and Appeals (OMHA) in Miami, Florida. Julie Miles, Clinical Appeals Specialist, of Novocare and Debra M. Parrish, Esq., appeared on behalf of the appellant and testified. Exhibits 1-3 were admitted into evidence without objection.

ISSUES

The issue on appeal is whether the electrical stim cancer treatment provided by the Appellant to the beneficiary on January 27, 2018, February 27, 2018 and March 27, 2018, is covered by Medicare, and, if not, who is responsible for the non-covered charges?

FINDINGS OF FACT

Correspondence contained in the file from CMS following an inquiry requesting an informal benefit category determination (BCD) for the NovoTTF – 100A system states that CMS believed that the NovoTTF-100A system fell within the DME benefit category. (Ex. 2, p. 76)

On November 24, 2016 the beneficiary underwent a post-op tumor resection MRI of the brain with and without contrast to evaluate for residual. The MRI revealed fluid, hemorrhage and postoperative changes, a decrease in the left temporal lobe and a decrease in mass effect of the left temporal lobe upon the brain stem. (Ex. 2, pp. 34-35)

On December 1, 2016, the beneficiary was evaluated by Dr. REDACTED for a newly diagnosed high-grade glioma. It was noted that he was status post craniotomy with gross total resection on November 23, 2016. The recommended follow up treatment consisted of radiation therapy and chemotherapy. (Ex. 2, pp. 31-33).

The radiation treatment summary dated January 30, 2017 states that the beneficiary was diagnosed with glioblastoma, left temporal and that he received external beam radiation using IMRT with concurrent temozolomide from December 15, 2016 to January 30, 2017. (Ex. 2, pp. 29-30)

The February 7, 2017 medical records state that the beneficiary was one week post treatment and that he improved over several days, with a few bad days. He was off dexamethasone and Optune would be tried. (Ex. 2, p. 28)

A prescription for Optune (formerly NovoTTF-100A System) was certified on February 7, 2017, August 23, 2017 and January 31, 2018, due to a diagnosis of left malignant neoplasm of temporal lobe. The duration of the use of Optune was 6 months. (Ex. 2, pp. 8-10)

The Optune Device and accessories were delivered to the beneficiary and a technical review was conducted on February 27, 2017. (Ex. 2, pp. 23, 27)

Invoices for the treatment were submitted for services dates of January 27, 2018, February 27, 2018 and March 27, 2018. (Ex. 2, pp. 5-7)

LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014 and the Act, Title VXIII, § 1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. See 70 Fed. Reg. 36386, 36387 (June 23, 2005), as amended by 76 Fed. Reg. 19995 (April 11, 2011). The ALJs within OMHA issue the binding decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

For requests filed in calendar year 2014, the minimum amount remaining in controversy required for an ALJ hearing is \$140.00 (following application of any co-insurance or deductible). The Act, Title XVIII, § 1869(b)(1)(E), 77 Fed. Reg. 59618 (Sept. 28, 2012). The request for hearing is timely if filed within sixty days after receipt of a QIC decision. See 42 CFR §405.1014(b)(1).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a).

The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a de novo review of each claim at issue. The Administrative Procedure Act, § 557 and 70 Fed. Reg. 36386 (June 23, 2005).

A de novo review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient documentary evidence in accordance with Medicare rules). See e.g., Sections 1814(a)(1), 1815(b), and 1833(e) of Title VXIII of the Act; see also 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. 42 C.F.R. § 405.1018. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Statutes and Regulations

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§ 1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services. Section 1831 established the Supplemental Medical Insurance Program for the aged and disabled under Part B.

Section 1832 of the Act and 42 CFR §410.3 establish the scope of benefits that are provided to beneficiaries under the Medicare Part B insurance program. Under §1832(a)(2)(B) of the Act, an individual is entitled to have payment made on his behalf for medical and other health services furnished by a provider of services or by others under arrangement with them made by a provider of services.

Under the authority of Section 1842(a)(1)(A) of the Act, the Secretary of the Department of Health and Human Services is authorized to enter into contracts with private entities, or carriers, for the day-to-day operations of the program.

Section 1833(e) of the Act precludes payment to any providers of services unless “there has been furnished such information as may be necessary in order to determine the amounts due such provider.”

Section 1862 of the Act provides that only items and services that are reasonable and necessary for the diagnosis and treatment of illness or injury are covered under the Medicare program.

Section 1879 of the Act limits the liability of the beneficiary and providers of services if the services are found to be not medically reasonable and necessary under §1862(a)(1)(A). Payment will only be made pursuant to this section if neither the beneficiary nor the provider knew or could reasonably have been expected to know that the services were not covered.

Also considered are: 42 CFR §424.5 (provider, supplier, or beneficiary must supply sufficient information to determine whether payment is due and the amount); 42 CFR §405.1062 (ALJ's will give substantial deference to Local Coverage Determinations (LCDs), Local Medical Review Policy's (LMRPs), or Center for Medicare Services (CMS) program guidance when applicable and if they do not follow the policy they must explain why in their decision), 42 CFR §405.1028, (admission of documentation following a QIC decision) and 42 CFR §411.406 (criteria for determining that a provider, practitioner, or supplier knew that services were excluded from coverage as custodial care or as not reasonable and necessary.).

A. Policy and Guidance

The Health Care Procedure Coding System (HCPCS) is the alpha-numeric coding system developed by the Health Care Financing Administration (now CMS) for processing, screening, identifying and paying Medicare claims.

In the absence of a national policy, or to further clarify a national policy, Medicare contractors make coverage decisions in their area about what items or services are reasonable and necessary. These Local Coverage Determinations (LCDs), or Local Medical Review Policies (LMRPs), are developed to specify criteria that describe whether an item or service is covered and under what clinical circumstances it is considered to be reasonable and necessary. Contractors develop LCDs or LMRPs by considering medical literature, the advice of local medical societies and medical consultants, public comments, and comments from the provider community. The Administrative Law Judge is not bound by the LCD or LMRP. *Erringer v Thompson* 189 F. Supp 2d 984 (D. Ariz. 2001) *aff'd*, 371 F.3d 625 (9th Cir. 2004). However, the LCDs and LMRPs are given substantial deference as an interpretive guide in evaluating whether the coverage criteria for services rendered have been satisfied. Specific to this case is the Medicare Program Integrity Manual, Pub. 100-08, Chapter 3, Section 3.3.2.1.

The undersigned ALJ gave substantial deference to LCD L34823.

Analysis

The QIC denied the claim stating that the medical documentation received indicates that the beneficiary had a diagnosis of glioblastoma, however, the medical documentation did not support a need for the device. There was insufficient documentation to quantify the effects of the device for the beneficiary. Therefore, payment cannot be made. (Ex. 1, p. 4)

In this case, the Medicare statutes and regulations were substantially satisfied for Medicare payment of the assigned claims.

Appellant testified that the beneficiary was diagnosed with glioblastoma brain cancer in November 2016, a rare form of cancer, that it is a highly aggressive form of cancer and the survival rate is approximately 10 months. The Appellant further testified that the FDA approved a device to deliver TTFT treatment, finding it to be safe and effective for treatment of glioblastomas. The beneficiary's treating physician prescribed TTFT treatment and the Optune device and accessories were delivered to the beneficiary. The Appellant stated that providing an exact quantification of effectiveness is not a requirement for Medicare coverage, but that the beneficiary's extended survival rate, beyond the average 10 months is an attestation to the effectiveness of the treatment. REDACTED was diagnosed in November 2016 and died in December 2018.

The medical record indicates that correspondence contained in the file from CMS following an inquiry requesting an informal benefit category determination (BCD) for the NovoTTF – 100A system states that CMS believed that the NovoTTF-100A system fell within the DME benefit category. (Ex. 2, p. 76) On November 24, 2016 the beneficiary underwent a post-op tumor

resection MRI of the brain with and without contrast to evaluate for residual. The MRI revealed fluid, hemorrhage and postoperative changes, a decrease in the left temporal lobe and a decrease in mass effect of the left temporal lobe upon the brain stem. (Ex. 2, pp. 34-35) On December 1, 2016, the beneficiary was evaluated by Dr. REDACTED for a newly diagnosed high-grade glioma. It was noted that he was status post craniotomy with gross total resection on November 23, 2016. The recommended follow up treatment consisted of radiation therapy and chemotherapy. (Ex. 2, pp. 31-33). A prescription for Optune (formerly NovoTTF-100A System) was certified on February 7, 2017, August 23, 2017 and January 31, 2018, due to a diagnosis of left malignant neoplasm of temporal lobe. The duration of the use of Optune was 6 months. (Ex. 2, pp. 8-10) The Optune Device and accessories were delivered to the beneficiary and a technical review was conducted on February 27, 2017. (Ex. 2, pp. 23, 27)

Under these circumstances, the undersigned finds that the electrical stim cancer treatment provided by the Appellant to the beneficiary on January 27, 2018, February 27, 2018 and March 27, 2018, was reasonable and necessary and met Medicare coverage criteria. Appellant is entitled to payment.

CONCLUSIONS OF LAW

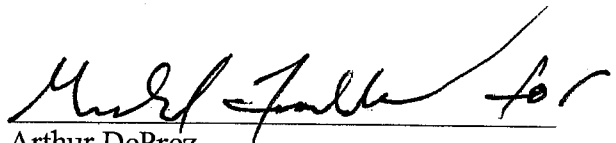
The undersigned finds that Appellant is entitled to payment for the electrical stim cancer treatment provided by the Appellant to the beneficiary on January 27, 2018, February 27, 2018 and March 27, 2018, based upon the substantial and detailed medical record and because the services are not otherwise excluded from Medicare coverage under § 1862 of the Act. Accordingly, the provider should be reimbursed under the provisions of Title XVIII of the Act.

ORDER

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: JAN 25 2019


Arthur DePrez
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of:

OMHA Appeal No.: **1-6983357272**

Enrollee:

Medicare: **Part C**

HICN: *******5321A**

Before: **Donna Dickens**
Administrative Law Judge

ON-THE-RECORD DECISION

After carefully considering the evidence and arguments presented in the record and at hearing, a **FULLY FAVORABLE** on-the-record decision is entered for the Appellant/Enrollee,

Procedural History

The Enrollee, , sought pre-approval for Medicare, Part C coverage of an electrical stimulation device. The Enrollee's Medicare Advantage Plan ("MA Plan"), HUMANA INSURANCE COMPANY (HUMANA), denied coverage through redetermination. MAXIMUS, a Medicare Qualified Independent Contractor ("QIC"), upheld the denials upon reconsideration review on November 9, 2017.

By correspondence received November 16, 2017, Appellant requested a hearing before an Administrative Law Judge ("ALJ") of the Office of Medicare Hearings and Appeals ("OMHA").

Following review of the record, the undersigned finds a favorable decision is warranted. Thus, the undersigned is issuing this decision without a hearing as permitted under 42 C.F.R. §405.1038(a). All exhibits were admitted into the record.

Issues

The issue presented is whether the MA Plan is required to cover the Enrollee's electrical stimulation device under Medicare, Part C.

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

1. The Enrollee, an 80-year old male, has a medical history significant for glioblastoma ("GBM"). (Ex. 2, p. 4). He also has a medical history significant for anemia, atrial fibrillation, coronary artery disease, prostate cancer, cataracts, hyperlipidemia, hypertension, inguinal hernia without mention of obstruction or gangrene, unilateral or unspecified, and osteoarthritis. *Id.*
2. On October 18, 2017, the Enrollee's physician, M.D., prepared a correspondence to the MA Plan. (Ex. 2, p. 1).
 - a. According to the correspondence, the Enrollee initially presented with hiccups followed by confusion. *Id.*
 - b. Neuroimaging revealed a right temporal lobe mass. *Id.* He underwent a subtotal resection on June 2, 2017 and pathology was consistent with GBM. *Id.*
 - c. The Enrollee underwent chemo therapies from July 6, 2017 through July 24, 2017. *Id.*
 - d. As of October 18, 2017, the Enrollee continued to experience random visual hallucinations. *Id.*
 - e. As a result of the aforementioned, the physician decided to prescribe Optune for the Enrollee in combination with temozolomide as the best treatment to treat the Enrollee's GBM. *Id.*
 - f. The physician explains that the alternating electric field therapy (Optune) and adjuvant temozolomide is now an NCCN Category 2A recommendation following postoperative standard brain radiation therapy. *Id.*
3. The record included an Article from the Journal of the American Medical Association titled *Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide Alone for Glioblastoma* with the original print date December 15, 2015. (Ex. 2, pp. 28-37). The record also included an Article from the National Comprehensive Cancer Network ("NCCN") Clinical Practice Guidelines in Oncology for Central Nervous System Cancers, Version 1, 2016. (Ex. 2, pp. 38-41).
4. Optune received pre-market approval from the FDA for recurrent GBM in April 2011 based on the results of a large randomized controlled trial of patients with recurrent GBM comparing Optune as a monotherapy to standard chemotherapy used in recurrent GBM. (Ex. 2, p. 1). In 2015, Optune received pre-market approval from the FDA for newly diagnosed GBM in combination with temozolomide after standard surgical resection and radiation therapy. (Ex. 2, p. 2).
5. The QIC denied coverage finding that the MA plan was not required to pre-approve the electrical stimulation device. (Ex. 1, p. 5). The QIC provided that tumor treatment field therapy (E0766) is not considered medically reasonable or necessary, pursuant to LCD L34823. *Id.*

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act (Act) § 1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. See 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

A hearing before an ALJ is only available if the remaining amount in controversy is \$150 or more for requests filed in calendar year 2015. See 79 Fed. Reg. 57934 (Sep. 26, 2014). The request for hearing is timely if filed within sixty days after receipt of the reconsideration determination. See 20 C.F.R. § 404.933(b)(1).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor; however, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision, the Appellant will be notified and it will be considered an issue at hearing. 42 C.F.R. § 405.1032(a).

The ALJ may decide a case on the record and not conduct an oral hearing if the evidence in the hearing record supports a finding in favor of appellant(s) on every issue, or if the Appellant and all parties indicate in writing that they do not wish to appear before the ALJ at oral hearing. 42 C.F.R. § 405.1038.

The burden of proving each element of a Medicare claim lies with the Appellant by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). See Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; 42 C.F.R. § 424.5(a)(6), 42 C.F.R. § 405.1018, 42 C.F.R. § 405.1028, and 42 C.F.R. § 405.1030. All laws and regulations pertaining to the Medicare and Medicaid programs, including, but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations, are binding on ALJ's. 42 C.F.R. § 405.1063.

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. See 42 C.F.R. § 405.1018, 42 C.F.R. § 405.1028 and 42 C.F.R. § 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. See 42 C.F.R. § 405.1018(d).

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into the record. *Id.*

C. Standard of Review

The ALJ conducts a de novo review of each claim at issue and issues a decision based on the hearing record. 42 C.F.R. § 405.1000(d) and Section 557 of the Administrative Procedure Act. De novo review requires the ALJ to review and evaluate the evidence without regard to the findings of prior determinations on the claim and make an independent assessment relying upon the evidence and controlling laws.

II. Principles of Law

A. Social Security Act

The Medicare Program, Title XVII of the Act (42 U.S.C. §§1395-139ggg) is administered through CMS. The Secretary of the Department of Health and Human Services is authorized to enter into contracts with private entities for the day-to-day operations of the program, §1842(a)(1)(A) of the Act.

The MA program (Part C of the Act) provides that a MA organization offering a MA plan must provide enrollees, at a minimum, with all basic Medicare-covered services by furnishing the benefits directly or through arrangements, or by paying for the benefits. Basic benefits are benefits defined as “all Medicare covered services, except hospice services.” Mandatory supplemental benefits are defined as “services not covered by Medicare that an MA enrollee must purchase as part of an MA plan that are paid for in full, directly by (or on behalf of) Medicare enrollees, in the form of premiums or cost sharing. Optional supplemental benefits are defined as “health services not covered by Medicare that are purchased at the option of the MA enrollee and paid for in full, directly by (or on behalf of) the Medicare enrollee, in the form of premiums or cost sharing. These services may be grouped or offered individually.” §1852(a) of the Act, 42 CFR §422.100

MA organization health plans must provide coverage for all services that are covered by Part A and Part B of Medicare (if the enrollee is entitled to benefits under both parts) or by Medicare Part B (if entitled only under Part B). Further, MA's must comply with national coverage determinations as promulgated by the Centers for Medicare and Medicaid Services. 42 CFR §422.101. MA organizations must disclose to each beneficiary enrolling in a MA plan offered by the organization a detailed content of plan description, including, but not limited to, the plan's service area, benefits, access, out-of-area coverage, emergency coverage, premiums and cost sharing (such as co-payments, deductibles and coinsurance). This information must be offered at the time of enrollment and at least annually after that, in a clear, accurate and standardized form. 42 CFR 422.111. MA organizations may specify the networks of providers from whom enrollees may obtain services as long as the MA organization ensures that all covered services, including additional or supplemental services contracted for by (or on behalf of) the Medicare enrollee, are available and accessible under the plan with reasonable promptness and in a manner

which assures continuity in the provision of benefits. §1852 (d) of the Act; 42 U.S.C § 1395w-22(d); 42 CFR §422.112.

Notwithstanding any other provision of Title XVIII of the Act, Section 1862(a) of the Act [42 U.S.C. § 1395y(a)(1)(A)] limits the payments that may be made under Part A or Part B, stating in pertinent part that, “no payment may be made under Part A or Part B for any expenses incurred for items or services — (1)(A) which . . . are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member . . .” *Id.*; See also 42 CFR § 411.15(k)(1.) Additionally, § 1833(e) of the Act [42 U.S.C. § 1395l(e)] prohibits Medicare payment for any claim that lacks such information as may be necessary in order to determine the amounts due such provider.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that no rule, requirement, or statement of policy can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program unless it is promulgated as a regulation by CMS, with the only exception being national coverage determinations (NCDs). See 42 CFR § 405.1060. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance describing the criteria for coverage of selected items and services in the form of manuals and local coverage determinations (LCDs), respectively.

i. LCD L34823: Tumor Treatment Field Therapy (TTFT)

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements.

The purpose of a Local Coverage Determination (LCD) is to provide information regarding “reasonable and necessary” criteria based on Social Security Act § 1862(a)(1)(A) provisions.

In addition to the “reasonable and necessary” criteria contained in this LCD there are other payment rules, which are discussed in the following documents, that must also be met prior to Medicare reimbursement:

- The LCD-related Standard Documentation Requirements Article, located at the bottom of this policy under the Related Local Coverage Documents section.
- The LCD-related Policy Article, located at the bottom of this policy under the Related Local Coverage Documents section.
- Refer to the Supplier Manual for additional information on documentation requirements.
- Refer to the DME MAC web sites for additional bulletin articles and other publications related to this LCD.

For the items addressed in this LCD, the “reasonable and necessary” criteria, based on Social Security Act §1862(a)(1)(A) provisions, are defined by the following coverage indications, limitations and/or medical necessity.

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

C. MA Plan

HUMANA INSURANCE COMPANY (HUMANA)’s 2017 Evidence of Coverage details the services covered by the MA Plan (Ex.1).

Analysis

The Appellant has satisfied the jurisdictional requirements for a hearing before OMHA as the amount in controversy exceeds the requisite amount and the request for hearing was received within 60 days of the reconsideration determination. Having considered the evidence and argument of record, the undersigned finds the request for pre-approval for the electrical stimulation device, should be granted under the Medicare program.

In the instant case, the Enrollee, an 80-year old male, has a medical history significant for GBM. He also has a medical history significant for anemia, atrial fibrillation, coronary artery disease, prostate cancer, cataracts, hyperlipidemia, hypertension, inguinal hernia without mention of obstruction or gangrene, unilateral or unspecified, and osteoarthritis. According to the Enrollee’s physician’s correspondence dated October 18, 2017, the Enrollee initially presented with hiccups followed by confusion. Neuroimaging revealed a right temporal lobe mass. He underwent a subtotal resection on June 2, 2017 and pathology was consistent with GBM. The Enrollee underwent chemo therapies from July 6, 2017 through July 24, 2017. As of October 18, 2017, the Enrollee continued to experience random visual hallucinations. As a result of the aforementioned, the physician decided to prescribe Optune for the Enrollee in combination with temozolomide as the best treatment to treat the Enrollee’s GBM. The physician explains that the alternating electric field therapy (Optune) and adjuvant temozolomide is now an NCCN Category 2A recommendation following postoperative standard brain radiation therapy.

The undersigned has conducted a de novo review of the administrative record and agrees with the Appellant. Pursuant to the applicable LCD, “Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary;” however, the ALJ agrees that the LCD is not binding and does not take into account the educated opinions in the related medical field. The ALJ has taken into account the medical articles presented by the Enrollee’s physician and his assertion that “[a]t the St. Elizabeth Healthcare Cancer Center Optune has been employed successfully for patients such as [Enrollee], and we have achieved excellent results.” The ALJ also notes that based on the material presented, the Enrollee suffers from an orphan disease with limited treatment options, and that Optune in combination with temozolomide appears to be medically necessary and appropriate given the Enrollee’s serious medical condition and that this option has been acknowledged as a safe and effective procedure. Therefore, the undersigned ALJ concludes that pre-approval for the electrical stimulation device should be granted under the Medicare program.

Conclusions of Law


The pre-approval for the electrical stimulation device should be granted under the Medicare program.

ORDER

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated: JAN 26 2018


Donna Dickens
Administrative Law Judge



U.S. Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appellant:	OMA Appeal No: 1-7835229033
Enrollee:	Medicare Part B
MIDN:	
Date(s) of Service: Sept. 25, 2017 – Dec. 25, 2017	Before: J. Keith Essmyer, Jr. U.S. Administrative Law Judge
Claim Amount(s): \$21,000 per month	

DECISION

After careful consideration of the entire record, applicable laws, regulations, rulings, and policies, I enter a **FAVORABLE** decision for Appellant.

PROCEDURAL HISTORY

Novocure, Inc. (Novocure) filed multiple claims for a **NovoTTF-100A System (NovoTTFS) (E0766)**¹ (Exhibit 1, Pages 23-26, 41).

The Medicare Administrative Contractor (MAC) denied the claims because tumor treatment field therapy (TTFT) is not considered medically reasonable and necessary under the applicable Local Coverage Determination (LCD) (Exhibit 1, Page 15).

The Qualified Independent Contractor (QIC) denied the claims because there is insufficient documentation to show the effectiveness of the NovoTTFS (Exhibit 1, Pages 4-5).

A telephone hearing was held on **November 6, 2018**. Debra M. Parrish, Esq. (Representative), Julie Miles, RN (Ms. Miles), and Dan McCoy (Mr. McCoy) appeared for Appellant.

LEGAL FRAMEWORK

Title XVIII of the Social Security Act (Act) contains the controlling statutes; Title 42 of the Code of Federal Regulations (CFR) contains the controlling regulations; Medicare Program Integrity Manual (MPIM), Chapter 5, Section 5.7 (effective March 1, 2008), MPIM, Chapter 13, Section 13.5.1 (effective April 9, 2004), Medicare Benefit Policy Manual (MBPM), Chapter 15, Section 110.1 (effective April 1, 2013), MBPM, Chapter 16, Section 20 (effective October 1, 2003), Medicare Claims Processing Manual (MCPM), Chapter 20, Sections 20, 20.4, and 30.2 (each effective October 1, 2003), and MCPM, Chapter 23, Section 60.3 (effective January 1, 2017) contain applicable policy; Noridian Healthcare Solutions, LLC (Noridian)² Local Coverage Determination (LCD) L34823, *Tumor Treatment Field Therapy (TTFT)* (effective January 1, 2017), and Noridian Policy Article (PA) A52711, *Tumor Treatment Field Therapy (TTFT)* (effective January 1, 2017), contain applicable coverage requirements.

¹ The **NovoTTF-100A System (NovoTTFS)** is a portable, wearable tumor treatment field therapy device (TTFT-device) manufactured by Novocure that delivers TTFT to targeted tumors and is available only by prescription (Exhibit 2, Pages 74-123).

² Noridian is the **DME MAC** for the region covering the Beneficiary's state of residence. Noridian LCDs and PAs are available at [Noridianmedicare.com](https://med.noridianmedicare.com/) at <https://med.noridianmedicare.com/>.

Section 1862 of the Social Security Act (commonly cited as 42 United States Code (USC) section 1395y) provides that no payment may be made under Medicare Part A or Part B for items or services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member (42 USC §1395y(a)(1)(a)).

Section 1879 of the Social Security Act (commonly cited as 42 USC section 1395pp) provides that payment for non-covered services can be made if the individual receiving the services and the provider of the services do not know or have reason to know that the services are not covered by Medicare (42 USC §§1395pp(a)(1)-(2)). The individual receiving the services is not liable for payment to the provider for the services if (s)he does not know or have reason to know that the services are not covered by Medicare (42 USC §1395pp(a)(2); *See also*: 42 CFR §411.402(a)(2); 42 CFR §411.404(a)-(c) and (e)(1)).

The Administrative Law Judge (ALJ) conducts a *de novo* review and issues a decision based on the record (42 CFR §405.1000(d))³. *Local Coverage Determination* (LCD) means a decision by a Medicare carrier to cover a particular service under Medicare Part A or Part B (42 CFR §400.202, definition of LCD). Although not bound by LCDs or Medicare program policies, the ALJ must give these substantial deference (42 CFR §405.1062(a)). If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed (42 CFR §405.1062(b)).

For hearing requests filed on or after January 1, 2018, a party does not have a right to an ALJ hearing unless the remaining **amount in controversy (AIC)** is **\$160** after reduction for any Medicare payment already made and any applicable deductible and coinsurance amounts (42 CFR §405.1006(b) and (d)(1)(i)-(ii); *Federal Register*, Vol. 82, No. 188, Pg. 45592-45593, Sept. 29, 2017, *effective January 1, 2018*).

Medicare Part B pays for DME if used in the patient's home or in an institution that is used as a home (42 CFR §410.38(a)). *Durable medical equipment (DME)* means equipment, furnished by a supplier or a home health agency that meets the following conditions: (1) Can withstand repeated use; (2) Effective with respect to items classified as DME after January 1, 2012, has an expected life of at least 3 years; (3) Is primarily and customarily used to serve a medical purpose; (4) Generally is not useful to an individual in the absence of an illness or injury; (5) Is appropriate for use in the home (42 CFR §414.202 (definition of DME)).

Services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member are excluded from Medicare coverage (42 CFR §411.15(k)(1)).

Items and services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member are not covered (MBPM, Ch. 16, §20).

For DME and/or supplies to be covered by Medicare, the patient's medical record must contain sufficient documentation substantiating the need for the DME/supplies. A physician's order, certificate of medical necessity (CMN), or physician's statement by itself is not sufficient to document medical necessity for the DME/supplies (MPIM, Ch. 5 §5.7).

A service is considered reasonable and necessary if it is: safe and effective; not experimental or investigational; and appropriate as to duration and frequency (MPIM, Ch. 13, §13.5.1).

³ A new and independent review not bound by any previous decision(s) issued in a case.

DME is equipment which: Can withstand repeated use; Is primarily and customarily used to serve a medical purpose; Generally is not useful to a person in the absence of an illness or injury; and, Is appropriate for use in the home. All requirements of the definition must be met before an item can be considered to be durable medical equipment MBPM, Ch. 15, §110.1).

Section 1834 of the Social Security Act requires the use of fee schedules under Medicare Part B for reimbursement of DME, beginning January 1 1989. Payment is limited to the lower of the actual charge for the equipment or the fee established (MCPM, Ch. 20, §20).

The DME fee schedule file provided by the Centers for Medicare and Medicaid Services (CMS) contains HCPCS codes and related prices subject to the DME fee schedules, including application of any update factors and any changes to the national limited payment amounts. The file also does not include fees for items for which fee schedule amounts are not established. See MCPM, Chapter 23 for a description of pricing for these items (MCPM, Ch. 20, §20.4).

For DME items requiring frequent and substantial servicing, MACs pay the fee schedule amounts on a rental basis until medical necessity ends. MACs cannot pay for purchase of this type of DME (MCPM, Ch. 20, §30.2).

The DME MACs and Part B MACs must gap-fill the DMEPOS fee schedule for items for which charge data were unavailable during the fee schedule data base year using the fee schedule amounts for comparable equipment, using properly calculated fee schedule amounts from a neighboring DME MAC or Part BMAC area, or using supplier price lists with prices in effect during the fee schedule data base year (MCPM, Ch. 23, §60.3).

Contractors send their gap-fill information to CMS. After receiving the gap-filled base fees each year, CMS develops national fee schedule floors and ceilings and new fee schedule amounts for these codes and releases them as part of the July update file each year and during the quarterly updates (MCPM, Ch. 23, §60.3).

TTFT (E0766) will be denied as not medically reasonable and necessary (L34823).

TTFT devices are covered under the DME benefit (A52711).

Code (E0766) describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers (A52711).

Code (E0766) is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling (A52711).

ISSUES

1. Are the NovoTTFS services covered by Medicare?
2. If not covered, can payment be made or liability waived for the services under Section 1879 of the Social Security Act?

FINDINGS OF FACT

Based on the record, I make the following findings of fact (FOF):

1. Progress notes, dated November 7, 2016, indicate Appellant is a 73-year old woman diagnosed with glioblastoma (GBM)⁴ who is status post (s/p) partial resection and chemotherapy. The notes also indicate Appellant started using the NovoTTFS as part of her treatment plan in 2015, and her GBM has remained relatively stable (Exhibit 2, Pages 23-24).
2. Prescriptions, signed and dated by the treating oncologist, indicate Appellant is prescribed the NovoTTFS to treat GMB (Exhibit 2, Pages 1-3).
3. A letter of medical necessity (LMN), signed and dated by treating oncologist on May 17, 2016, indicates there are very few treatment options available for patients with GBM and that the NovoTTFS is the most appropriate treatment for Appellant. The LMN also indicates Appellant has exhausted all other FDA⁵-approved treatment options (Exhibit 2, Pages 4-5).

ANALYSIS

Medicare does not covered services considered not medically reasonable and necessary (42 USC §1395y (a)(1)(a); 42 CFR §411.15(k)(1); MBPM, Ch. 16, §20; MPIM, Ch. 13, §13.5.1). Medicare Part B pays for DME used in the home (42 CFR §410.38(a)). For DME to be covered by Medicare, the patient's medical record must contain sufficient documentation substantiating the need for the DME. A physician's order, CMN, or physician's statement by itself is not sufficient to document medical necessity for DME (MPIM, Ch. 5 §5.7). TTFT (E0766) will be denied as not medically reasonable and necessary (L34823). TTFT devices are covered under the DME benefit (A52711). The ALJ is not bound by LCDs but must give LCDs substantial deference (42 CFR §405.1062(a)). If an ALJ declines to follow an LCD in a particular case, the ALJ decision must explain the reasons for not following the LCD (42 CFR §405.1062(b)).

Appellant is diagnosed with GBM and has been using the NovoTTFS as part of her treatment plan since 2015. Appellant is prescribed the NovoTTFS because she has exhausted all other FDA-approved treatment options (FOF 1-3). Ms. Miles testified the NovoTTFS in combination with or following chemotherapy is the most appropriate treatment option for patients like Appellant. Ms. Miles also testified clinical trials have shown TTFT extends the life of GBM patients and that Appellant has lived two (2) years past the normal life expectancy for a GBM patient. Mr. McCoy testified treatment with the NovoTTFS has become the standard of care for GBM patients. The Representative stated Appellant was told she only had 10 months to live when she was diagnosed with GBM in 2015, and argues the record demonstrates TTFT is medically reasonable and necessary for Appellant and supports departing from the LCD to allow coverage for the NovoTTFS.

⁴ Glioblastoma (GBM) is an aggressive type of cancer that can occur in the brain or spinal cord. GBM tumors form from cells called astrocytes that support nerve cells. GBM can occur at any age but tends to occur more often in older adults, and can cause worsening headaches, nausea, vomiting and seizures. GBM, also known as glioblastoma multiforme, can be very difficult to treat and a cure is often not possible. Treatments may slow progression of the cancer and reduce signs and symptoms (Source: Mayo Clinic at <https://www.mayoclinic.org/diseases-conditions/glioblastoma/cdc-20350148>).

⁵ United States Food and Drug Administration

I am persuaded by the Representative's argument. Medicare covers medically reasonable and necessary DME. The applicable LCD (L34823) simply declares TTFT not medically reasonable and necessary without giving any reasons or explanation for this decision. L34823 is skeletal and arbitrary and lacks any articulable reasoning by Noridian as to why it determined TTFT to be a non-covered service^{6,7}. I decline to follow such an LCD in the face of overwhelming evidence that TTFT is a medically reasonable and necessary part of Appellant's treatment plan. The studies provided by Appellant show that TTFT is a medically accepted treatment and when combined with traditional chemotherapy prolongs the life of GBM patients (Exhibit 2, Pages 135-187; *see also* Exhibit 3, CD). Many prestigious medical institutions also consider TTFT in combination with chemotherapy to be a medically accepted treatment for GBM patients^{8,9}. I therefore find TTFT devices meet Medicare's coverage criteria for medically reasonable and necessary DME¹⁰. I also find the NovoTTFS services provided to Appellant are covered by Medicare

Having found the NovoTTFS services covered, I need not address any remaining issue(s) in this case.

CONCLUSIONS OF LAW and ALJ ORDER

The NovoTTFS services (E0766) provided to Appellant on September 25, 2017, through December 25, 2017, are covered by Medicare.

The services will be covered as a rental DME at the Medicare allowable rate^{11, 12, 13}.

⁶ Medicare coverage of TTFT devices (E0766) is left to the discretion of the carrier (i.e. DME MAC) (CPT Codebook 2017).

⁷ Healthcare providers utilize HCPCS/CPT codes to report medical services performed on patients to Medicare carriers. Healthcare Common Procedure Coding System (HCPCS) consist of Level I CPT (Current Procedural Terminology) codes and Level II codes. CPT codes are defined in the American Medical Association's (AMA) CPT Manual. Level II codes are defined by CMS (NCCI Manual, Ch. 1, Section A, Page I-5).

⁸ TTFT uses an electrical field to disrupt the GBM tumor cells' ability to multiply. TTFT involves applying adhesive pads to the scalp. The pads are connected to a portable device that generates the electrical field. TTFT is combined with chemotherapy and may be recommended after radiation (Source: Mayo Clinic at <https://www.mayoclinic.org/diseases-conditions/glioblastoma/cdc-20350148>).

⁹ TTFT provides a noninvasive option for patients with a recurrence of GBM for whom treatments like surgery, radiation, or cancer drug therapy did not produce sufficient results. TTFT has been shown to have little effect on normal adult brain cells; and, since TTFT is only applied to the brain, it does not affect rapidly multiplying cells in the rest of the body. The most commonly reported side effect from TTFT is a mild to moderate scalp rash (beneath the electrodes) (Source: Cancer Treatment Centers of America at <https://www.cancercenter.com/brain-cancer/optune/>).

¹⁰ DME is equipment which: Can withstand repeated use; Is primarily and customarily used to serve a medical purpose; Generally is not useful to a person in the absence of an illness or injury; and, Is appropriate for use in the home. All requirements of the definition must be met before an item can be considered to be durable medical equipment MBPM, Ch. 15, §110.1). The applicable PA indicates that TTFT devices are covered under the DME benefit (A52711) and the record includes a letter from CMS indicating the devices fall within the DME benefit category (Exhibit 2, Pages 69-73). There is no doubt the prescribed NovoTTFS is DME and the record supports it is medically reasonable and necessary DME.

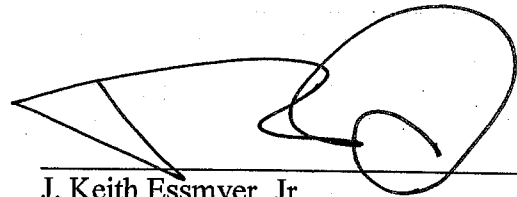
¹¹ TTFT devices (E0677) are in the frequent and substantial service payment category and cannot be purchased but must be billed as a rental item (MCPM, Ch. 20, §30.2; A52711).

¹² There is no charge data for TTFT devices (E0677) in the 2017 and 2018 DME fee schedules published by CMS (Source: CMS.gov at <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/DMEPOSFeeSched/DMEPOS-Fee-Schedule.html>). Noridian may use a gap-fill DME schedule to determine the Medicare allowable amount(s) for the NovoTTFS services at issue in this appeal. A gap-fill DME schedule uses the fee schedule amounts for comparable

This decision is based on a *de novo* review of the record. Appellant's appeal and the claims in this case will be processed in accordance with this decision¹⁴.

Dated:

DEC 10 2018



J. Keith Essmyer, Jr.
U.S. Administrative Law Judge

equipment, properly calculated fee schedule amounts from a neighboring DME MAC or Part B MAC area, or supplier price lists with prices in effect during the fee schedule data base year (MCPM, Ch. 23, §60.3).

¹³ Standard documentation requirements for DME claims are listed in Noridian PA A55426, *Standard Documentation Requirements for All Claims Submitted to DME MACs* (applicable effective dates: June 1, 2017, November 20, 2017, and December 21, 2017).

¹⁴ A recent Medicare Appeals Council (Council) decision (M-17-6802) reversed my decision in which I granted coverage for a surgical procedure by departing from the applicable LCD that listed the procedure as a non-covered service. The Council determined the Medicare Advantage (MA) plan (i.e. Medicare Part C plan) was not legally or factually obligated to cover the procedure regardless of the enrollee's personal situation because the LCD is binding on the plan and does not contemplate coverage of the procedure in any circumstances. The Council noted the LCD itself indicated that "LCDs are based on the strongest evidence available." Council decisions are not precedential authority or binding on other cases (42 CFR §405.1130) unless designated precedential (42 CFR §401.109; 42 CFR 405.1063(B)). To date, the Council's decision has not been designated precedential and may only be viewed as persuasive authority. I, however, do not find the Council's decision persuasive. Like the LCD in this case (L34823), the Council's analysis is skeletal, citing only 42 CFR §422.101(b)(3)) as a reason to deny coverage because MA plans are bound by LCDs. The Council fails to address an MA plan's obligation when an ALJ exercises his or her authority to depart from an LCD and finds Medicare coverage is available. This would have been a more helpful analysis given the fact MA plans are required to cover items and services that Original Medicare covers (i.e. Medicare Part A and Part B), which occurs when an ALJ has a sound basis to depart from an LCD to allow coverage. Unlike the LCD in the Council's decision, L34824 does not contain a self-assuring proclamation that it is based on the strongest evidence available. To the contrary, L34824 has no statements at all explaining Noridian's reasoning for determining TTFT is not medically reasonable and necessary; and, I refuse to deny coverage to Appellant based on such an LCD when the record overwhelming supports TTFT is a medically necessary part of her treatment plan for GBM. I also note, this is a Medicare Part B case, and coverage is allowed under Part B when an ALJ has good reason(s) for refusing to follow an LCD (42 CFR §405.1062(a)-(b)).



U.S. Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appellant:	ALJ Appeal No: 1-7092982181
Enrollee:	Medicare Part C
HICN: ***-**-0418A	Before: J. Keith Essmyer, Jr.
Coverage Request Date: November 15, 2017	U.S. Administrative Law Judge
Projected Value Amount: \$21,000 per month¹	

DECISION

After careful consideration of the entire record, applicable laws, regulations, rulings, and policies, I enter a **FAVORABLE** decision for Appellant.

PROCEDURAL HISTORY

Appellant filed a coverage request for the following service(s): NovoTTF-100A System (NovoTTF) (E0766)² (Exhibit 1, Pages 10, 19-21).

Blue Cross Blue Shield of Michigan (BCBSM) and the Independent Review Entity (IRE) denied the request because tumor treatment field therapy (TTFT) is not considered medically reasonable and necessary under the applicable Local Coverage Determination (LCD) (Exhibit 1, Page 4-5, 15-16, 54-57).

A telephone hearing was held on January 31, 2018. Appellant appeared at the hearing with _____, M.D., _____, Stephanie Hale, Esq. (Ms. Hale), and Justin Kelly, R.N. (Kelly). Camiel Riggins (Ms. Riggins) and James Leisen, M.D. (Dr. Leisen) appeared for BCBSM³.

LEGAL FRAMEWORK

Title XVIII of the Social Security Act (Act) contains the controlling statutes; Title 42 of the Code of Federal Regulations (CFR) contains the controlling regulations; Medicare Program Integrity Manual (MPIM), Chapter 5, Section 5.7 (effective March 1, 2008), MPIM, Chapter 13, Section 13.5.1 (effective April 9, 2004), Medicare Benefit Policy Manual (MBPM), Chapter 15, Section 110.1 (effective April 1, 2013), MBPM, Chapter 16, Section 20 (effective October 1, 2003), Medicare Claims Processing Manual (MCPM), Chapter 20, Sections 20, 20.4, and 30.2 (each effective October 1, 2003), and MCPM, Chapter 23, Section 60.3 (effective January 1, 2017) contain applicable policy; BCBSM's Evidence of Coverage (EOC)

¹ This is the commercial rate for the requested device (Hearing Testimony). The commercial rate is used as the projected value amount for this case to demonstrate the amount in controversy (AIC) requirements for an ALJ hearing are met.

² The NovoTTF-100A System (NovoTTF) is a portable, wearable tumor treatment field therapy device (TTFT-device) manufactured by Novocure that delivers TTFT to targeted tumors and is available only by prescription (Exhibit 2, Pages 31-88).

³ All parties received the Notice of Hearing (NOH) issued by the Office of Medicare Hearings and Appeals (OMHA) in this case and appeared at the hearing. No party, however, submitted a written response to the NOH (Exhibit 4).

(effective January 1, 2017, through December 31, 2017), Noridian Healthcare Solutions (Noridian)⁴ Local Coverage Determination (LCD) L34823, *Tumor Treatment Field Therapy (TTFT)* (effective January 1, 2017), and Noridian Policy Article (PA) A52711, *Tumor Treatment Field Therapy (TTFT)* (effective January 1, 2017), contains applicable coverage requirements.

Section 1862 of the Social Security Act (commonly cited as 42 United States Code (USC) section 1395y) provides that no payment may be made under Medicare Part A or Part B for items or services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member (42 USC §1395y(a)(1)(a)).

Unless otherwise provided under the regulations for Medicare Part C appeals, the regulations found in Part 405 of Title 42 of the Code of Federal Regulations (CFR) for Medicare Part A and Part B appeals apply to the administrative review and hearing processes for Part C appeals (42 CFR §422.562(d))^{5, 6}.

If the amount remaining in controversy after reconsideration meets the threshold requirement established annually by the Secretary of the Department of Health and Human Services (Secretary), any party to the reconsideration, except the Medicare Advantage (MA) organization, who is dissatisfied with the reconsideration determination has a right to a hearing before an Administrative Law Judge (ALJ) (42 CFR 422.600(a)). The amount remaining in controversy is computed in accordance with [42 CFR Part 405] (42 CFR 422.600(b)). If the basis for the appeal is the MA organization's refusal to provide services, the projected value of those services is used to compute the amount remaining in controversy (42 CFR 422.600(c)).

MA plan means health benefits coverage offered under a policy or contract by an MA organization that includes a specific set of health benefits offered at a uniform premium and uniform level of cost-sharing to all Medicare beneficiaries residing in the service area of the MA plan (42 CFR §422.2 definition of MA plan). *MA plan enrollee* is a MA eligible individual who has elected an MA plan offered by an MA organization (42 CFR 422.2 definition of MA plan enrollee). MA plans at a minimum include basic benefits, which are all Medicare covered services, except hospice services (42 CFR §422.100(c)(1)). MA plans are reviewed and approved annually by the Centers for Medicare and Medicaid Services (CMS) (42 CFR §§422.254 and 422.255).

MA plans must comply with written coverage decisions of local MACs with jurisdiction for claims in the geographic area the plan services (42 CFR §422.101(b)(3)).

For hearing requests filed on or after January 1, 2017, a party does not have a right to an ALJ hearing unless the remaining amount in controversy is \$160 after reduction for any Medicare payment already made and any applicable deductible and coinsurance amounts (42 CFR §405.1006(b) and (d)(1)(i)-(ii); *Federal Register*, Vol. 81, No. 185, Pg. 65651-65653, Sept. 23, 2016, *effective January 1, 2017*).

⁴ Noridian is the Medicare durable medical equipment (DME) Medicare Administrative Contractor (MAC) (DME MAC) for the region covered by Appellant's Medicare Advantage (MA) plan. Noridian LCDs and PAs are available at [Noridianmedicare.com](https://med.noridianmedicare.com/web/jddme) at <https://med.noridianmedicare.com/web/jddme>.

⁵ Part 405 and Part 422 of Title 42 of the Code of Federal Regulations (CFR) contain the controlling regulations.

⁶ The regulations for Medicare Part C grievances, organization determinations, and appeals are found in 42 CFR Part 422, Subpart M.

The Administrative Law Judge (ALJ) conducts a *de novo* review and issues a decision based on the record (42 CFR §405.1000(d))⁷. *Local Coverage Determination* (LCD) means a decision by a Medicare carrier to cover a particular service under Medicare Part A or Part B (42 CFR §400.202, definition of LCD). Although not bound by LCDs or Medicare program policies, the ALJ must give these substantial deference (42 CFR §405.1062(a)). If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed (42 CFR §405.1062(b)).

Medicare Part B pays for DME if used in the patient's home or in an institution that is used as a home (42 CFR §410.38(a)). *Durable medical equipment (DME)* means equipment, furnished by a supplier or a home health agency that meets the following conditions: (1) Can withstand repeated use; (2) Effective with respect to items classified as DME after January 1, 2012, has an expected life of at least 3 years; (3) Is primarily and customarily used to serve a medical purpose; (4) Generally is not useful to an individual in the absence of an illness or injury; (5) Is appropriate for use in the home (42 CFR §414.202 (definition of DME)).

Services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member are excluded from Medicare coverage (42 CFR §411.15(k)(1)).

Items and services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member are not covered (MBPM, Ch. 16, §20).

For DME and/or supplies to be covered by Medicare, the patient's medical record must contain sufficient documentation substantiating the need for the DME/supplies. A physician's order, certificate of medical necessity (CMN), or physician's statement by itself is not sufficient to document medical necessity for the DME/supplies (MPIM, Ch. 5 §5.7).

A service is considered reasonable and necessary if it is: safe and effective; not experimental or investigational; and appropriate as to duration and frequency (MPIM, Ch. 13, §13.5.1).

DME is equipment which: Can withstand repeated use; Is primarily and customarily used to serve a medical purpose; Generally is not useful to a person in the absence of an illness or injury; and, Is appropriate for use in the home. All requirements of the definition must be met before an item can be considered to be durable medical equipment MBPM, Ch. 15, §110.1).

Section 1834 of the Social Security Act requires the use of fee schedules under Medicare Part B for reimbursement of DME, beginning January 1 1989. Payment is limited to the lower of the actual charge for the equipment or the fee established (MCPM, Ch. 20, §20).

The DME fee schedule file provided by the Centers for Medicare and Medicaid Services (CMS) contains HCPCS codes and related prices subject to the DME fee schedules, including application of any update factors and any changes to the national limited payment amounts. The file also does not include fees for items for which fee schedule amounts are not established. See MCPM, Chapter 23 for a description of pricing for these items (MCPM, Ch. 20, §20.4).

For DME items requiring frequent and substantial servicing, MACs pay the fee schedule amounts on a rental basis until medical necessity ends. MACs cannot pay for purchase of this type of DME (MCPM, Ch. 20, §30.2).

⁷ A new and independent review not bound by any previous decision(s) issued in a case.

The DME MACs and Part B MACs must gap-fill the DMEPOS fee schedule for items for which charge data were unavailable during the fee schedule data base year using the fee schedule amounts for comparable equipment, using properly calculated fee schedule amounts from a neighboring DME MAC or Part B MAC area, or using supplier price lists with prices in effect during the fee schedule data base year (MCPM, Ch. 23, §60.3).

Contractors send their gap-fill information to CMS. After receiving the gap-filled base fees each year, CMS develops national fee schedule floors and ceilings and new fee schedule amounts for these codes and releases them as part of the July update file each year and during the quarterly updates (MCPM, Ch. 23, §60.3).

TTFT (E0766) will be denied as not medically reasonable and necessary (L34823).

TTFT devices are covered under the DME benefit (A52711).

Code (E0766) describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers (A52711).

Code (E0766) is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling (A52711).

BCBSM covers everything that Original Medicare covers (EOC, Ch. 4, §2.1, Page 56).

Medicare covered services must be provided according to Medicare coverage guidelines (EOC, Ch. 4, §2.1, Page 56).

Services must be medically necessary. "Medically necessary" means the services, supplies, or drugs are needed for the prevention, diagnosis, or treatment of [an enrollee's] medical condition and meet accepted standards of medical practice (EOC, Ch. 4, §2.1, Page 56).

BCBSM covers all medically necessary DME covered by Original Medicare (EOC, Ch. 4, Medical Benefits Chart (MBC), Page 72).

ISSUES

Is BCBSM required to grant Appellant's coverage request?

FINDINGS OF FACT

Based on the record, I make the following findings of fact (FOF):

1. Appellant is enrolled in a MA plan administered by BCBSM (Exhibit 1, Pages 10-12)⁸.
2. A surgical pathology report, dated July 27, 2017, indicates Appellant has glioblastoma (GBM)⁹ in the temporal lobe (Exhibit 2, Pages 17-22).

⁸ Appellant testified she has renewed her enrollment in the MA plan for 2018 (Hearing Audio).

3. Office visit notes, dated October 17, 2017, indicate Appellant is a 49-year old woman diagnosed with GBM who is experiencing a rapidly deteriorating mental status, confusion, difficulty waking up, slurred speech, and facial droop. The notes also indicate Appellant underwent an emergency craniotomy on July 27, 2017, and her pathology is consistent with GBM. The notes further indicate Appellant will be started on standard adjuvant chemotherapy with temozolomide¹⁰ for 6-12 cycles and that she is an ideal candidate to use the NovoTTF as part of her treatment plan (Exhibit 2, Pages 8-14).
4. A prescription, signed and dated by Dr. _____ on November 13, 2017, indicates Appellant is prescribed the NovoTTF to treat GMB (Exhibit 2, Page 4).
5. A letter of medical necessity (LMN), signed and dated by Dr. _____ on November 29, 2017, indicates there are very few treatment options available for patients with GBM and that the NovoTTF in combination with temozolomide is the most appropriate treatment for Appellant. The LMN also indicates the Henry Ford Health System (HFHS) has successfully used the NovoTTF in treating patients with GBM (Exhibit 2, Pages 1-3).

ANALYSIS

BCBSM does not cover services Original Medicare considers not medically reasonable and necessary (42 USC §1395y (a)(1)(a); 42 CFR §411.15(k)(1); MBPM, Ch. 16, §20; MPIM, Ch. 13, §13.5.1; EOC, Ch. 4, §2.1, Page 56). Medicare Part B pays for DME used in the home (42 CFR §410.38(a)). BCBSM covers medically necessary DME covered by Original Medicare (EOC, Ch. 4, MBC, Page 72). For DME to be covered by Medicare, the patient's medical record must contain sufficient documentation substantiating the need for the DME. A physician's order, CMN, or physician's statement by itself is not sufficient to document medical necessity for DME (MPIM, Ch. 5 §5.7). TTFT (E0766) will be denied as not medically reasonable and necessary (L34823). TTFT devices are covered under the DME benefit (A52711). MA plans must adhere to LCDs (42 CFR §422.101(b)(3)). The ALJ is not bound by LCDs but must give LCDs substantial deference (42 CFR §405.1062(a)). If an ALJ declines to follow an LCD in a particular case, the ALJ decision must explain the reasons for not following the LCD (42 CFR §405.1062(b)).

Appellant is enrolled in a MA plan administered by BCBSM. Appellant is diagnosed with GBM and is experiencing rapid mental deterioration, confusion, difficulty waking up, slurred speech, and facial droop. Dr. _____ prescribed the NovoTTF in combination with temozolomide to treat Appellant's GBM and believes this is the most appropriate treatment for her (FOF 1-5). Appellant testified she is suffering from fatigue and is having difficulty coping with standard chemotherapy treatments. _____ testified Appellant cannot take a full dose of temozolomide during her chemotherapy treatments and that the NovoTTF is one of the few options available to her. Dr. _____ testified the NovoTTF in combination with chemotherapy is the most appropriate treatment option for patients like Appellant. Dr. _____ also testified clinical trials have shown TTFT extends the life of GBM patients. Mr. Kelly testified the NovoTTF is FDA

⁹ **Glioblastoma (GBM)** is an aggressive type of cancer that can occur in the brain or spinal cord. GBM tumors form from cells called astrocytes that support nerve cells. GBM can occur at any age but tends to occur more often in older adults, and can cause worsening headaches, nausea, vomiting and seizures. GBM, also known as glioblastoma multiforme, can be very difficult to treat and a cure is often not possible. Treatments may slow progression of the cancer and reduce signs and symptoms (Source: Mayo Clinic at <https://www.mayoclinic.org/diseases-conditions/glioblastoma/cdc-20350148>).

¹⁰ **Temozolomide** (brand name: **Temodar**) is a chemotherapy drug used to treat GBM (Source: Chemocare at <http://chemocare.com/chemotherapy/drug-info/Temozolomide.aspx>).

approved¹¹ and has been shown to improve the life expectancy of GBM patients. Ms. Hale argues the record demonstrates TTFT for Appellant is medically reasonable and necessary and supports departing from the LCD to allow coverage for the NovoTTF prescribed by Dr.

Dr. Leisen testified BCBSM denied Appellant's coverage request because it is bound by the applicable LCD (L34823) that indicates TTFT is not medically reasonable and necessary. Dr. Leisen also testified he does not know why Noridian considers TTFT not medically reasonable and necessary.

I am persuaded by Appellant's argument that the NovoTTF recommended by her treating physician is a medically reasonable and necessary service. Neither BCBSM nor Original Medicare (i.e. Medicare Part A and Part B) covers items or services that are not medically reasonable and necessary. Both BCBSM and Original Medicare cover medically reasonable and necessary DME. L34823 simply declares TTFT not medically reasonable and necessary without giving any reasons or explanation for this decision. L34823 is skeletal and arbitrary and lacks any articulable reasoning by Noridian as to why it determined TTFT to be a non-covered service^{12, 13}. I decline to follow such an LCD in the face of overwhelming evidence that TTFT is a medically reasonable and necessary part of Appellant's treatment plan. The studies provided by Appellant show that TTFT is a medically accepted treatment and when combined with traditional chemotherapy prolongs the life of GBM patients (Exhibit 2, Pages 122-185). Many prestigious medical institutions also consider TTFT in combination with chemotherapy to be a medically accepted treatment for GBM patients^{14, 15, 16}. I therefore find TTFT devices meet Medicare's coverage criteria for medically reasonable and necessary DME¹⁷. I further find BCBSM is required to grant Appellant's coverage request for the prescribed NovoTTF and must cover the device under the DME benefit of her MA plan.

¹¹ See also Exhibit 2, Pages 26-30.

¹² Medicare coverage of TTFT devices (E0677) is left to the discretion of the carrier (i.e. DME MAC) (CPT Codebook 2017).

¹³ Healthcare providers utilize HCPCS/CPT codes to report medical services performed on patients to Medicare carriers. Healthcare Common Procedure Coding System (HCPCS) consist of Level I CPT (Current Procedural Terminology) codes and Level II codes. CPT codes are defined in the American Medical Association's (AMA) CPT Manual. Level II codes are defined by CMS (NCCI Manual, Ch. 1, Section A, Page I-5).

¹⁴ TTFT uses an electrical field to disrupt the GBM tumor cells' ability to multiply. TTFT involves applying adhesive pads to the scalp. The pads are connected to a portable device that generates the electrical field. TTFT is combined with chemotherapy and may be recommended after radiation (Source: Mayo Clinic at <https://www.mayoclinic.org/diseases-conditions/glioblastoma/cdc-20350148>).

¹⁵ TTFT provides a noninvasive option for patients with a recurrence of GBM for whom treatments like surgery, radiation, or cancer drug therapy did not produce sufficient results. TTFT has been shown to have little effect on normal adult brain cells; and, since TTFT is only applied to the brain, it does not affect rapidly multiplying cells in the rest of the body. The most commonly reported side effect from TTFT is a mild to moderate scalp rash (beneath the electrodes) (Source: Cancer Treatment Centers of America at <https://www.cancercenter.com/brain-cancer/optune/>).

¹⁶ See also FOF 5.

¹⁷ DME is equipment which: Can withstand repeated use; Is primarily and customarily used to serve a medical purpose; Generally is not useful to a person in the absence of an illness or injury; and, Is appropriate for use in the home. All requirements of the definition must be met before an item can be considered to be durable medical equipment MBPM, Ch. 15, §110.1). The applicable PA indicates that TTFT devices are covered under the DME benefit (A52711) and the record includes a letter from CMS indicating the devices fall within the DME benefit category (Exhibit 2, Page 25). There is no doubt the prescribed NovoTTF is DME and the record supports it is medically reasonable and necessary DME.

CONCLUSIONS OF LAW and ALJ ORDER

BCBSM is required to grant Appellant's coverage request for the NovoTTF (E0677). BCBSM will cover the NovoTTF as a rental DME benefit under Appellant's MA plan at the **Medicare allowable rate** until medical necessity ends^{18, 19, 20}.

This decision is based on a *de novo* review of the record. Appellant's coverage request will be processed in accordance with this decision²¹.

Dated: **FEB 23 2018**



J. Keith Essmyer, Jr.
U.S. Administrative Law Judge

¹⁸ TTFT devices (E0677) are in the frequent and substantial service payment category and cannot be purchased but **must be billed as a rental item** (MCPM, Ch. 20, §30.2; A52711).

¹⁹ There is no charge data for TTFT devices (E0677) in the 2017 and 2018 DME fee schedules published by CMS (Source: CMS.gov at <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/DMEPOSFeeSched/DMEPOS-Fee-Schedule.html>). **BCBSM may request Noridian provide a gap-fill DME schedule for the NovoTTF using the fee schedule amounts for comparable equipment, using properly calculated fee schedule amounts from a neighboring DME MAC or Part B MAC area, or using supplier price lists with prices in effect during the fee schedule data base year** (MCPM, Ch. 23, §60.3).

²⁰ Standard documentation requirements for DME claims are listed in Noridian PA A55426, *Standard Documentation Requirements for All Claims Submitted to DME MACs* (effective December 21, 2017).

²¹ A recent Medicare Appeals Council (Council) decision (**M-17-6802**) reversed my decision in which I granted coverage for a surgical procedure by departing from the applicable LCD that listed the procedure as a non-covered service. The Council determined the MA plan was not legally or factually obligated to cover the procedure regardless of the enrollee's personal situation because the LCD is binding on the plan and does not contemplate coverage of the procedure in any circumstances. The Council noted the LCD itself indicated that "LCDs are based on the strongest evidence available." Council decisions are not precedential authority or binding on other cases (42 CFR §405.1130) unless designated precedential (42 CFR §401.109; 42 CFR 405.1063(B)). To date, the Council's decision has not been designated precedential and may only be viewed as persuasive authority. I, however, do not find the Council's decision persuasive. Like the LCD in this case (L34823), the Council's analysis is skeletal, citing only 42 CFR §422.101(b)(3)) as a reason to deny coverage because MA plans are bound by LCDs. The Council fails to address an MA plan's obligation when an ALJ exercises his or her authority to depart from an LCD and finds Medicare coverage is available. This would have been a more helpful analysis given the fact MA plans are required to cover items and services that Medicare covers, which occurs when an ALJ has a sound basis to depart from an LCD to allow coverage. Unlike the LCD in the Council's decision, L34824 does not contain a self-assuring proclamation that it is based on the strongest evidence available. To the contrary, L34824 has no statements at all explaining Noridian's reasoning for determining TTFT is not medically reasonable and necessary; and, I refuse to deny coverage to Appellant based on such an LCD when the record overwhelming supports TTFT is a medically necessary part of her treatment plan for GBM.



**U.S. Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida**

Appellant: Enrollee: HICN: Coverage Request Date: November 6, 2017 Projected Value Amount: \$21,000 per month¹	ALJ Appeal No: 1-7142315942 Medicare Part C Before: J. Keith Essmyer, Jr. U.S. Administrative Law Judge
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DECISION

After careful consideration of the entire record, applicable laws, regulations, rulings, and policies, I enter a **FAVORABLE** decision for Appellant.

PROCEDURAL HISTORY

Appellant filed a coverage request for the following service(s): NovoTTF-100A System (NovoTTF) (E0766)² (Exhibit 1, Pages 21-104).

Blue Cross Blue Shield of Minnesota (BCBSM) and the Independent Review Entity (IRE) denied the request because tumor treatment field therapy (TTFT) is not considered medically reasonable and necessary under the applicable Local Coverage Determination (LCD) (Exhibit 1, Page 4-5, 13-14, 19-20).

A telephone hearing was held on February 20, 2018. Appellant appeared at the hearing with Michael W. Ruff, M.D. (Dr. Ruff), Stephanie Hale, Esq. (Ms. Hale), and Justin Kelly, R.N. (Kelly). Jessica Ammons Flynn and Nicole Holloway, R.N. (collectively, "Plan-Rep") appeared for BCBSM.

LEGAL FRAMEWORK

Title XVIII of the Social Security Act (Act) contains the controlling statutes; Title 42 of the Code of Federal Regulations (CFR) contains the controlling regulations; Medicare Program Integrity Manual (MPIM), Chapter 5, Section 5.7 (effective March 1, 2008), MPIM, Chapter 13, Section 13.5.1 (effective April 9, 2004), Medicare Benefit Policy Manual (MBPM), Chapter 15, Section 110.1 (effective April 1, 2013), MBPM, Chapter 16, Section 20 (effective October 1, 2003), Medicare Claims Processing Manual (MCPM), Chapter 20, Sections 20, 20.4, and 30.2 (each effective October 1, 2003), and MCPM, Chapter 23, Section 60.3 (effective January 1, 2017) contain applicable policy; BCBSM's Evidence of Coverage (EOC) (effective January 1, 2017, through December 31, 2017), CGS Administrators, LLC (CGS)³ Local Coverage

¹ This is the commercial rate for the requested device (Hearing Testimony). The commercial rate is used as the projected value amount for this case to demonstrate the amount in controversy (AIC) requirements for an ALJ hearing are met.

² The NovoTTF-100A System (NovoTTF) is a portable, wearable tumor treatment field therapy device (TTFT-device) manufactured by Novocure that delivers TTFT to targeted tumors and is available only by prescription (Exhibit 1, Pages 38-44).

³ CGS is the Medicare durable medical equipment (DME) Medicare Administrative Contractor (MAC) (DME MAC) for the region covered by Appellant's Medicare Advantage (MA) plan. CGS LCDs and PAs are available at [CGSmedicare.com](https://www.cgsmedicare.com/jb/) at <https://www.cgsmedicare.com/jb/>.

Determination (LCD) L34823, *Tumor Treatment Field Therapy (TTFT)* (effective January 1, 2017), and CGS Policy Article (PA) A52711, *Tumor Treatment Field Therapy (TTFT)* (effective January 1, 2017), contains applicable coverage requirements.

Section 1862 of the Social Security Act (commonly cited as 42 United States Code (USC) section 1395y) provides that no payment may be made under Medicare Part A or Part B for items or services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member (42 USC §1395y(a)(1)(a)).

Unless otherwise provided under the regulations for Medicare Part C appeals, the regulations found in Part 405 of Title 42 of the Code of Federal Regulations (CFR) for Medicare Part A and Part B appeals apply to the administrative review and hearing processes for Part C appeals (42 CFR §422.562(d))^{4, 5}.

If the amount remaining in controversy after reconsideration meets the threshold requirement established annually by the Secretary of the Department of Health and Human Services (Secretary), any party to the reconsideration, except the Medicare Advantage (MA) organization, who is dissatisfied with the reconsideration determination has a right to a hearing before an Administrative Law Judge (ALJ) (42 CFR 422.600(a)). The amount remaining in controversy is computed in accordance with [42 CFR Part 405] (42 CFR 422.600(b)). If the basis for the appeal is the MA organization's refusal to provide services, the projected value of those services is used to compute the amount remaining in controversy (42 CFR 422.600(c)).

MA plan means health benefits coverage offered under a policy or contract by an MA organization that includes a specific set of health benefits offered at a uniform premium and uniform level of cost-sharing to all Medicare beneficiaries residing in the service area of the MA plan (42 CFR §422.2 definition of MA plan). *MA plan enrollee* is a MA eligible individual who has elected an MA plan offered by an MA organization (42 CFR 422.2 definition of MA plan enrollee). MA plans at a minimum include basic benefits, which are all Medicare covered services, except hospice services (42 CFR §422.100(c)(1)). MA plans are reviewed and approved annually by the Centers for Medicare and Medicaid Services (CMS) (42 CFR §§422.254 and 422.255).

MA plans must comply with written coverage decisions of local MACs with jurisdiction for claims in the geographic area the plan services (42 CFR §422.101(b)(3)).

For hearing requests filed on or after January 1, 2017, a party does not have a right to an ALJ hearing unless the remaining amount in controversy is \$160 after reduction for any Medicare payment already made and any applicable deductible and coinsurance amounts (42 CFR §405.1006(b) and (d)(1)(i)-(ii); *Federal Register*, Vol. 81, No. 185, Pg. 65651-65653, Sept. 23, 2016, effective January 1, 2017).

The Administrative Law Judge (ALJ) conducts a *de novo* review and issues a decision based on the record (42 CFR §405.1000(d))⁶. *Local Coverage Determination (LCD)* means a decision by a Medicare carrier to cover a particular service under Medicare Part A or Part B (42 CFR §400.202, definition of LCD). Although

⁴ Part 405 and Part 422 of Title 42 of the Code of Federal Regulations (CFR) contain the controlling regulations.

⁵ The regulations for Medicare Part C grievances, organization determinations, and appeals are found in 42 CFR Part 422, Subpart M.

⁶ A new and independent review not bound by any previous decision(s) issued in a case.

not bound by LCDs or Medicare program policies, the ALJ must give these substantial deference (42 CFR §405.1062(a)). If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed (42 CFR §405.1062(b)).

Medicare Part B pays for DME if used in the patient's home or in an institution that is used as a home (42 CFR §410.38(a)). *Durable medical equipment (DME)* means equipment, furnished by a supplier or a home health agency that meets the following conditions: (1) Can withstand repeated use; (2) Effective with respect to items classified as DME after January 1, 2012, has an expected life of at least 3 years; (3) Is primarily and customarily used to serve a medical purpose; (4) Generally is not useful to an individual in the absence of an illness or injury; (5) Is appropriate for use in the home (42 CFR §414.202 (definition of DME)).

Services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member are excluded from Medicare coverage (42 CFR §411.15(k)(1)).

Items and services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member are not covered (MBPM, Ch. 16, §20).

For DME and/or supplies to be covered by Medicare, the patient's medical record must contain sufficient documentation substantiating the need for the DME/supplies. A physician's order, certificate of medical necessity (CMN), or physician's statement by itself is not sufficient to document medical necessity for the DME/supplies (MPIM, Ch. 5 §5.7).

A service is considered reasonable and necessary if it is: safe and effective; not experimental or investigational; and appropriate as to duration and frequency (MPIM, Ch. 13, §13.5.1).

DME is equipment which: Can withstand repeated use; Is primarily and customarily used to serve a medical purpose; Generally is not useful to a person in the absence of an illness or injury; and, Is appropriate for use in the home. All requirements of the definition must be met before an item can be considered to be durable medical equipment MBPM, Ch. 15, §110.1).

Section 1834 of the Social Security Act requires the use of fee schedules under Medicare Part B for reimbursement of DME, beginning January 1 1989. Payment is limited to the lower of the actual charge for the equipment or the fee established (MCPM, Ch. 20, §20).

The DME fee schedule file provided by the Centers for Medicare and Medicaid Services (CMS) contains HCPCS codes and related prices subject to the DME fee schedules, including application of any update factors and any changes to the national limited payment amounts. The file also does not include fees for items for which fee schedule amounts are not established. See MCPM, Chapter 23 for a description of pricing for these items (MCPM, Ch. 20, §20.4).

For DME items requiring frequent and substantial servicing, MACs pay the fee schedule amounts on a rental basis until medical necessity ends. MACs cannot pay for purchase of this type of DME (MCPM, Ch. 20, §30.2).

The DME MACs and Part B MACs must gap-fill the DMEPOS fee schedule for items for which charge data were unavailable during the fee schedule data base year using the fee schedule amounts for comparable equipment, using properly calculated fee schedule amounts from a neighboring DME MAC or Part B MAC

area, or using supplier price lists with prices in effect during the fee schedule data base year (MCPM, Ch. 23, §60.3).

Contractors send their gap-fill information to CMS. After receiving the gap-filled base fees each year, CMS develops national fee schedule floors and ceilings and new fee schedule amounts for these codes and releases them as part of the July update file each year and during the quarterly updates (MCPM, Ch. 23, §60.3).

TTFT (E0766) will be denied as not medically reasonable and necessary (L34823).

TTFT devices are covered under the DME benefit (A52711).

Code (E0766) describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers (A52711).

Code (E0766) is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling (A52711).

BCBSM covers everything that Original Medicare covers (EOC, Ch. 4, §2.1, Pages 46-47).

Medicare covered services must be provided according to Medicare coverage guidelines (EOC, Ch. 4, §2.1, Pages 46-47).

Services must be medically necessary. "Medically necessary" means the services, supplies, or drugs are needed for the prevention, diagnosis, or treatment of [an enrollee's] medical condition and meet accepted standards of medical practice (EOC, Ch. 4, §2.1, Pages 46-47).

BCBSM covers all medically necessary DME covered by Original Medicare (EOC, Ch. 4, Medical Benefits Chart (MBC), Page 53).

ISSUES

Is BCBSM required to grant Appellant's coverage request?

FINDINGS OF FACT

Based on the record, I make the following findings of fact (FOF):

1. Appellant is enrolled in a MA plan administered by BCBSM (Exhibit 1, Pages 10-12)⁷.
2. A surgical pathology report, dated September 27, 2017, indicates Appellant has glioblastoma (GBM)⁸ in the frontal lobe (Exhibit 2, Pages 5-6).

⁷ Appellant testified he has renewed his enrollment in the MA plan for 2018 (Hearing Audio).

⁸ **Glioblastoma (GBM)** is an aggressive type of cancer that can occur in the brain or spinal cord. GBM tumors form from cells called astrocytes that support nerve cells. GBM can occur at any age but tends to occur more often in older adults, and can cause worsening headaches, nausea, vomiting and seizures. GBM, also known as glioblastoma multiforme, can be very difficult to treat

3. Office visit notes, dated November 3, 2017, indicate Appellant is a 77-year old man diagnosed with GBM who is experiencing fatigue and drooling from the left side of the mouth. The notes also indicate Appellant underwent a gross total surgical resection of the GBM lesion on September 22, 2017, and his pathology is consistent with GBM. The notes further indicate Appellant is completing chemotherapy and that he is an ideal candidate to use the NovoTTF as part of his treatment plan (Exhibit 2, Pages 7-8).
4. A prescription, signed and dated by Dr. Ruff on November 3, 2017, indicates Appellant is prescribed the NovoTTF to treat GMB (Exhibit 2, Pages 31-).
5. A letter of medical necessity (LMN), signed and dated by Dr. Ruff on November 29, 2017, indicates there are very few treatment options available for patients with GBM and that the NovoTTF in combination with temozolomide is the most appropriate treatment for Appellant. The LMN also indicates the Mayo Clinic has successfully used the NovoTTF in treating patients with GBM (Exhibit 1, Pages 15-17).

ANALYSIS

BCBSM does not cover services Original Medicare considers not medically reasonable and necessary (42 USC §1395y (a)(1)(a); 42 CFR §411.15(k)(1); MBPM, Ch. 16, §20; MPIM, Ch. 13, §13.5.1; EOC, Ch. 4, §2.1, Pages 46-47). Medicare Part B pays for DME used in the home (42 CFR §410.38(a)). BCBSM covers medically necessary DME covered by Original Medicare (EOC, Ch. 4, MBC, Page 53). For DME to be covered by Medicare, the patient's medical record must contain sufficient documentation substantiating the need for the DME. A physician's order, CMN, or physician's statement by itself is not sufficient to document medical necessity for DME (MPIM, Ch. 5 §5.7). TTFT (E0766) will be denied as not medically reasonable and necessary (L34823). TTFT devices are covered under the DME benefit (A52711). MA plans must adhere to LCDs (42 CFR §422.101(b)(3)). The ALJ is not bound by LCDs but must give LCDs substantial deference (42 CFR §405.1062(a)). If an ALJ declines to follow an LCD in a particular case, the ALJ decision must explain the reasons for not following the LCD (42 CFR §405.1062(b)).

Appellant is enrolled in a MA plan administered by BCBSM. Appellant is diagnosed with GBM and is experiencing fatigue and left side facial drooling. Dr. Ruff prescribed the NovoTTF in combination with temozolomide⁹ to treat Appellant's GBM and believes this is the most appropriate treatment for him (FOF 1-5). Dr. Ruff testified the NovoTTF in combination with chemotherapy is the most appropriate treatment option for patients like Appellant. Dr. Ruff also testified clinical trials have shown TTFT extends the life of GBM patients. Mr. Kelly testified the NovoTTF is FDA approved¹⁰ and has been shown to improve the life expectancy of GBM patients. Ms. Hale argues the record demonstrates TTFT for Appellant is medically reasonable and necessary and supports departing from the LCD to allow coverage for the NovoTTF prescribed by Dr. Ruff.

The Plan-Rep testified BCBSM denied Appellant's coverage request because it is bound by the applicable LCD (L34823) that indicates TTFT is not medically reasonable and necessary.

and a cure is often not possible. Treatments may slow progression of the cancer and reduce signs and symptoms (Source: Mayo Clinic at <https://www.mayoclinic.org/diseases-conditions/glioblastoma/cdc-20350148>).

⁹ **Temozolomide** (brand name: **Temodar**) is a chemotherapy drug used to treat GBM (Source: Chemocare at <http://chemocare.com/chemotherapy/drug-info/Temozolomide.aspx>).

¹⁰ See also Exhibit 2, Pages 13-17.

I am persuaded by Appellant's argument that the NovoTTF recommended by his treating physician is a medically reasonable and necessary service. Neither BCBSM nor Original Medicare (i.e. Medicare Part A and Part B) covers items or services that are not medically reasonable and necessary. Both BCBSM and Original Medicare cover medically reasonable and necessary DME. L34823 simply declares TTFT not medically reasonable and necessary without giving any reasons or explanation for this decision. L34823 is skeletal and arbitrary and lacks any articulable reasoning by CGS as to why it determined TTFT to be a non-covered service^{11, 12}. I decline to follow such an LCD in the face of overwhelming evidence that TTFT is a medically reasonable and necessary part of Appellant's treatment plan. The studies provided by Appellant show that TTFT is a medically accepted treatment and when combined with traditional chemotherapy prolongs the life of GBM patients (Exhibit 1, Pages 23-104). Many prestigious medical institutions also consider TTFT in combination with chemotherapy to be a medically accepted treatment for GBM patients^{13, 14, 15}. I therefore find TTFT devices meet Medicare's coverage criteria for medically reasonable and necessary DME¹⁶. I further find BCBSM is required to grant Appellant's coverage request for the prescribed NovoTTF and must cover the device under the DME benefit of his MA plan.

CONCLUSIONS OF LAW and ALJ ORDER

BCBSM is required to grant Appellant's coverage request for the NovoTTF (E0677). BCBSM will cover the NovoTTF as a rental DME benefit under Appellant's MA plan at the **Medicare allowable rate** until medical necessity ends^{17, 18, 19}.

¹¹ Medicare coverage of TTFT devices (E0677) is left to the discretion of the carrier (i.e. DME MAC) (CPT Codebook 2017).

¹² Healthcare providers utilize HCPCS/CPT codes to report medical services performed on patients to Medicare carriers. Healthcare Common Procedure Coding System (HCPCS) consist of Level I CPT (Current Procedural Terminology) codes and Level II codes. CPT codes are defined in the American Medical Association's (AMA) CPT Manual. Level II codes are defined by CMS (NCCI Manual, Ch. 1, Section A, Page I-5).

¹³ TTFT uses an electrical field to disrupt the GBM tumor cells' ability to multiply. TTFT involves applying adhesive pads to the scalp. The pads are connected to a portable device that generates the electrical field. TTFT is combined with chemotherapy and may be recommended after radiation (Source: Mayo Clinic at <https://www.mayoclinic.org/diseases-conditions/glioblastoma/cdc-20350148>).

¹⁴ TTFT provides a noninvasive option for patients with a recurrence of GBM for whom treatments like surgery, radiation, or cancer drug therapy did not produce sufficient results. TTFT has been shown to have little effect on normal adult brain cells; and, since TTFT is only applied to the brain, it does not affect rapidly multiplying cells in the rest of the body. The most commonly reported side effect from TTFT is a mild to moderate scalp rash (beneath the electrodes) (Source: Cancer Treatment Centers of America at <https://www.cancercenter.com/brain-cancer/optune/>).

¹⁵ See also FOF 5.

¹⁶ DME is equipment which: Can withstand repeated use; Is primarily and customarily used to serve a medical purpose; Generally is not useful to a person in the absence of an illness or injury; and, Is appropriate for use in the home. All requirements of the definition must be met before an item can be considered to be durable medical equipment MBPM, Ch. 15, §110.1). The applicable PA indicates that TTFT devices are covered under the DME benefit (A52711) and the record includes documentation indicating the devices fall within the DME benefit category (Exhibit 2, Pages 12-13). There is no doubt the prescribed NovoTTF is DME and the record supports it is medically reasonable and necessary DME.

¹⁷ TTFT devices (E0677) are in the frequent and substantial service payment category and cannot be purchased but **must be billed as a rental item** (MCPM, Ch. 20, §30.2; A52711).

¹⁸ There is no charge data for TTFT devices (E0677) in the 2017 and 2018 DME fee schedules published by CMS (Source: CMS.gov at <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/DMEPOSFeeSched/DMEPOS-Fee->

This decision is based on a *de novo* review of the record. Appellant's coverage request will be processed in accordance with this decision²⁰.

Dated: FEB 28 2018



J. Keith Essmyer, Jr.
U.S. Administrative Law Judge

Schedule.html). BCBSM may request CGS provide a gap-fill DME schedule for the NovoTFF using the fee schedule amounts for comparable equipment, using properly calculated fee schedule amounts from a neighboring DME MAC or Part B MAC area, or using supplier price lists with prices in effect during the fee schedule data base year (MCPM, Ch. 23, §60.3).

¹⁹ Standard documentation requirements for DME claims are listed in CGS PA A55426, *Standard Documentation Requirements for All Claims Submitted to DME MACs* (effective December 21, 2017).

²⁰ A recent Medicare Appeals Council (Council) decision (**M-17-6802**) reversed my decision in which I granted coverage for a surgical procedure by departing from the applicable LCD that listed the procedure as a non-covered service. The Council determined the MA plan was not legally or factually obligated to cover the procedure regardless of the enrollee's personal situation because the LCD is binding on the plan and does not contemplate coverage of the procedure in any circumstances. The Council noted the LCD itself indicated that "LCDs are based on the strongest evidence available." Council decisions are not precedential authority or binding on other cases (42 CFR §405.1130) unless designated precedential (42 CFR §401.109; 42 CFR 405.1063(B)). To date, the Council's decision has not been designated precedential and may only be viewed as persuasive authority. I, however, do not find the Council's decision persuasive. Like the LCD in this case (L34823), the Council's analysis is skeletal, citing only 42 CFR §422.101(b)(3)) as a reason to deny coverage because MA plans are bound by LCDs. The Council fails to address an MA plan's obligation when an ALJ exercises his or her authority to depart from an LCD and finds Medicare coverage is available. This would have been a more helpful analysis given the fact MA plans are required to cover items and services that Medicare covers, which occurs when an ALJ has a sound basis to depart from an LCD to allow coverage. Unlike the LCD in the Council's decision, L34824 does not contain a self-assuring proclamation that it is based on the strongest evidence available. To the contrary, L34824 has no statements at all explaining CGS's reasoning for determining TTFT is not medically reasonable and necessary; and, I refuse to deny coverage to Appellant based on such an LCD when the record overwhelming supports TTFT is a medically necessary part of his treatment plan for GBM.



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Irvine Field Office
Irvine, California

Appeal of: REDACTED	ALJ Appeal No.: 1-8071171566
Beneficiary:	Medicare Part: B
HICN: *	Before: Marilyn Mann Faulkner U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented in the record and at the hearing, a **FAVORABLE** decision is entered for REDACTED (Appellant and Beneficiary).
ED

Procedural History

The Appellant submitted claims for Optune Tumor Treatment Field Therapy (Optune TTFT), billed as electrical stimulation device used for cancer treatment (E0766) and provided to the Appellant on December 25, 2017; January 25, 2018; February 25, 2018; and March 25, 2018. CGS, the Medicare DME Administrative Contractor denied the claim on initial determination. The Appellant appealed the denial and CGS issued an unfavorable redetermination decision on April 30, 2018 (Exh. 1, pp. 13-14).

The Appellant requested reconsideration. On October 25, 2018, C2C Innovative Solutions, the Qualified Independent Contractor (QIC) issued an unfavorable decision finding the effectiveness of the device was not established. The provider, Novocure, was found responsible for the denied charges (Exh. 1, pp. 1-6).

The Appellant's timely filed request for Administrative Law Judge Hearing (ALJ) was received on November 7, 2018. The Appellant's request for hearing was timely filed. The amount in controversy meets the jurisdictional requirement. Accordingly, OMHA has jurisdiction to hear this appeal.

On December 19, 2018, a telephonic hearing was held at the Office of Medicare Hearings and Appeals (OMHA) Irvine Field Office in Irvine, California. Debra M. Parish, Attorney,

represented the Appellant. Julie Miles, R.N., appeared and testified as a witness on behalf of the Appellant. Exhibits 1 through 4 were admitted into evidence without objection.

Additional documentation from the MAC was submitted by the Appellant with the Request for Hearing and is included in the administrative record as part of Exhibit 4. Good cause exists for admission of the new evidence under 42 C.F.R. § 405.1018 at the ALJ level because the evidence is material to an issue addressed in the QIC's reconsideration and was not available until after the reconsideration request was submitted.

Issue

The issue to be decided is whether under the provisions of Title XVIII of the Social Security Act (Act) and implementing regulations, Medicare reimbursement can be made for Optune TTFT, billed as electrical stimulation device used for cancer treatment (E0766) and provided to the Appellant on December 25, 2017; January 25, 2018; February 25, 2018; and March 25, 2018.

Findings of Fact

The Appellant was diagnosed with a glioblastoma (GBM) in March 2017. She was treated with surgery, radiation, and chemotherapy. The Appellant experienced significant nausea as a result of the radiation and chemotherapy. The physician also noted other side effects and concerns regarding myelosuppression and the Appellant's declining white count as well as declining hemoglobin and hematocrit. The Appellant's physician prescribed Optune TTFT in July and November 2017 (Exh. 2, pp. 1-2, 23-24).

The August 7, 2018 letter from CGS, in response to a request for formal reconsideration of LCD L34823 for TTFT, acknowledged that LCD L34823 did not address newly diagnosed GBM. The MAC stated that it would complete the reconsideration of the LCD by September 18, 2018 (Exh. 4, pp. 18-20).

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Section 1869(b)(1)(A) of the Act.

In implementing this statutory directive, the Secretary has delegated authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *See* 74 Fed. Reg. 65296 (December 9, 2009). A hearing before an ALJ is available only if the remaining amount in controversy meets the jurisdictional amount. 42 Code

of Federal Regulations (C.F.R.) § 422.600(b). A request for hearing is timely if filed within sixty days after receipt of the reconsideration decision. 42 C.F.R. § 422.602(b).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in a party's favor. However, if evidence presented before the hearing causes the ALJ to question a fully favorable portion of the determination, the ALJ will notify the parties before the hearing and will consider it an issue at the hearing.

C. Standard of Review

An ALJ conducts a de novo review and issues a decision based on the hearing record. 42 C.F.R. § 405.1000(d).

II. Principles of Law

A. Statutes and Regulations

Section 1831 of the Act established the Supplementary Medical Insurance program (Medicare Part B) to provide medical insurance benefits for aged and disabled individuals who elect to enroll in the program. Section 1832 of the Act provides for coverage of medical and other health services. Section 410.10 of Title 42 of the C.F.R. allows Medicare coverage for medical and other health services, including medical supplies, appliances, and devices and durable medical equipment.

Section 1833(e) of the Act and Section 424.5(a)(6) of Title 42 of the C.F.R. provide that claims for payment must be supported by sufficient information and documentation.

Section 1862(a) of the Act provides that no payment may be made under Part A or Part B for any expenses incurred for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Section 1879 of the Act provides for the waiver of liability in certain instances when neither the provider nor beneficiary could have known, nor could be reasonably expected to have known, that the services would not be covered by Medicare.

42 C.F.R. § 405.1062 - Applicability of local coverage determinations and other policies not binding on the ALJ or attorney adjudicator and Council provides:

(a) ALJs and attorney adjudicators and the Council are not bound by LCDs, LMRPs, or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case.

(b) If an ALJ or attorney adjudicator or Council declines to follow a policy in a particular case, the ALJ or attorney adjudicator or Council decision must explain the reasons why the policy was not followed. An ALJ or attorney adjudicator or Council decision to disregard such policy applies only to the specific claim being considered and does not have precedential effect.

(c) An ALJ or attorney adjudicator or the Council may not set aside or review the validity of an LMRP or LCD for purposes of a claim appeal. An ALJ or the DAB may review or set aside an LCD (or any part of an LMRP that constitutes an LCD) in accordance with part 426 of this title.

42 C.F.R. §426.300 Review of LCDs, NCDs, and deemed NCDs provides:

(a) Upon the receipt of an acceptable LCD complaint as described in §426.400, an ALJ conducts a review of a challenged provision (or provisions) of an LCD using the reasonableness standard.

(b) Upon the receipt of an acceptable NCD complaint as described in §426.500, the Board conducts an NCD review of a challenged provision (or provisions) of an NCD using the reasonableness standard.

(c) The procedures established in this part governing the review of NCDs also apply in cases in which a deemed NCD is challenged.

42 C.F.R. §426.310 LCD and NCD reviews and individual claim appeals provide:

(a) LCD and NCD reviews are distinct from the claims appeal processes set forth in part 405, subparts G and H; part 417, subpart Q; and part 422, subpart M of this chapter.

(b) An aggrieved party must notify the ALJ or the Board, as appropriate, regarding the submission and disposition of any pending claim or appeal relating to the subject of the aggrieved party's LCD or NCD complaint. This reporting obligation continues through the entire LCD or NCD review process.

42 C.F.R. §426.320 Who may challenge an LCD or NCD.

(a) Only an aggrieved party may initiate a review of an LCD or NCD (including a deemed NCD), or provisions of an LCD or NCD by filing an acceptable complaint.

(b) Neither an ALJ nor the Board recognizes as valid any attempt to assign rights to request review under section 1869(f) of the Act.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than an National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (LMRPs) or Local Coverage Determinations (LCDs).

ALJs are not bound by LCDs, LMRPs, or CMS program guidance such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case.

CGS LCD L34823 – Tumor Treatment Field Therapy (TTFT) (Revision Effective Date Jan. 1, 2017) provides in part:

Coverage Indications, Limitations, and/or Medical Necessity

...

The purpose of a Local Coverage Determination (LCD) is to provide information regarding “reasonable and necessary” criteria based on Social Security Act § 1862(a)(1)(A) provisions.

In addition to the “reasonable and necessary” criteria contained in this LCD there are other payment rules, which are discussed in the following documents that must also be met prior to Medicare reimbursement:

For the items addressed in this LCD, the “reasonable and necessary” criteria, based on Social Security Act § 1862(a)(1)(A) provisions, are defined by the following coverage indications, limitations and/or medical necessity.

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. (Emphasis added).

...

HCPCS Codes

...

E0766 ELECTRICAL STIMULATION DEVICE USED FOR CANCER TREATMENT, INCLUDES ALL ACCESSORIES, ANY TYPE

...

The 2017 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Central Nervous System Cancers Version 1.2016 provides that alternating electric field therapy for glioblastoma is a category 2B recommendation (Exh. 1, p. 190).

Analysis

The QIC denied the claim at issue finding:

There is insufficient documentation to quantify the effects of the device for this Beneficiary. The currently published studies in the medical literature do not clearly document the effectiveness of this device (Exh. 1, p. 4).

In her brief and at the hearing, Debra Parrish argued that Glioblastoma is the most common but rare form of primary brain cancer that is highly aggressive with a survival of approximately ten months from the diagnosis date. She noted that Optune is durable medical equipment that delivers alternating electric fields or Tumor Treating Fields to the brain which slows the replication of cancer cells or stops their growth altogether. She emphasized that Optune is FDA approved for recurrent and newly diagnosed glioblastoma multiforme (GBM) brain tumors; that numerous peer-reviewed published studies have demonstrated the safety and efficacy of the Optune system and TTFT generally; and that Optune is incorporated in the NCCN guidelines (considered the gold standard for oncology management) for treatment of recurrent and newly-diagnosed GBM in combination with temozolomide. In addition, she pointed out that the Optune system has been certified at more than 800 cancer treatment centers, and has been prescribed by over 1200 physicians in 50 states, the District of Columbia, and Puerto Rico, for over 7200 patients. She argued that “[v]irtually every major payer in the United States covers the Optune system for individuals diagnosed with a glioblastoma. These payers include, among others, Highmark, Aetna, Anthem, Humana, Kaiser, UnitedHealthcare, Cigna, Harvard Pilgrim, Geisinger, HealthPartners, and several Blue Cross plans.” She further asserted that the LCD on its face does not reflect the current peer-reviewed literature, consensus of experts, and widespread adoption and is currently the subject of a reconsideration request based on its deficiencies. She also contended that DMAC medical directors have indicated the antiquated LCD does not apply to newly diagnosed glioblastoma and thus should not be used to preclude coverage.

Ms. Miles pointed out that the typical course of treatment for GBM is radiation and chemotherapy but that the Appellant experienced significant complications from chemotherapy and was hospitalized and required blood transfusions. She emphasized that the Appellant has received the tumor treatment field therapy for the dates of service indicated above since December 25, 2017 and as a result, has exceeded the average life expectancy for patients with GBM by one year. She asserted that, at present, the Appellant has no other treatment options; and that most major insurance carriers currently cover TTFT for GBM.

Application of LCD L34823

As noted above, ALJs are not bound by LCDs, LMRPs, or CMS program guidance such as program memoranda and manual instructions, but must give substantial deference to these policies if they are applicable to a particular case.

In the appeal at issue the Medicare Contractor, CGS, has stated that the cited LCD does not address coverage for newly diagnosed GBM – the Beneficiary’s diagnosis. Further, the MAC

stated that the Appellant had made a "valid request" for consideration of newly diagnosed GBM. The MAC stated that the review process would be completed by September 18, 2018. At the hearing, the Appellant's Attorney, Ms. Parrish, stated that due to a change in the rules for LCD review, she did not expect the completed review and/or new LCD to be issued before 2019.

Medical Effectiveness

The Optune®, formerly the NovoTTF-100A System, (Novocure, Portsmouth NH) was approved by the FDA in April 2011, as a novel device to treat adults age 22 years or older with GBM that recurs or progresses after receiving chemotherapy and radiation therapy. A supplemental FDA premarket approval was received in October 2015 for Optune™ with Temozolomide in adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy. For newly diagnosed GBM, Optune is not intended to be used as a substitute for standard treatments but rather as an adjunct therapy (<https://www.fda.gov/MedicalDevices/default.htm>).

Several major insurance carriers cover TTFT for GBM. For example, United Healthcare Electronic Tumor Treatment Field Therapy Policy, Effective Date: November 1, 2018 states in part:

The use of FDA approved devices to generate electric TTF is proven and medically necessary following radiologically-confirmed recurrence of GBM in the supratentorial region of the brain after initial chemotherapy and when ALL of the following criteria are met:

- ☐ The device is used as a monotherapy
- ☐ Individual has a KPS score of ≥ 60 ; and
- ☐ Individual or caregiver has been trained and is willing and able to apply the device daily; and
- ☐ Individual is willing to wear the device at least 18 hours daily.

When all of the above criteria are met for either newly diagnosed or recurrent GBM, an initial 3 months of electric TTF therapy will be approved.
<https://www.uhcprovider.com/content/dam/provider/docs/public/policies/comm-medical-drug/electric-tumor-treatment-field-therapy.pdf>

The Aetna Insurance Clinical Policy Bulletin states in part:

Aetna considers devices to generate electric tumor treatment fields (ETTF) and temozolomide medically necessary for persons with histologically confirmed glioblastoma (World Health Organization grade IV astrocytoma), after histologically or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. (Note: For recurrent glioblastoma, treatment until disease progression is considered medically necessary).

Aetna considers combination of devices to generate ETTF and temozolomide medically necessary as adjunctive treatment of newly-diagnosed histologically

confirmed supratentorial glioblastoma following standard treatments that include surgery, chemotherapy, and radiation therapy.

...

On October 5, 2015, the FDA approved an expanded indication for the Optune device (using alternating electrical fields called “tumor treatment fields” [TT Fields]) to treat patients with newly-diagnosed GBM. It is administered along with temozolomide (TMZ) following standard treatments that include surgery, chemotherapy, and radiation therapy. In the clinical study used to support the expanded indication, patients treated with the device and TMZ lived on average 3 months longer than those treated with the drug alone. Optune was initially approved in 2011 to treat patients with GBM that recurred or progressed after chemotherapy. With this expanded indication, Optune can be used as part of a standard treatment for GBM before the disease progresses. For newly diagnosed GBM, Optune is not intended to be used as a substitute for standard treatments, but rather as an adjunct therapy. The device is portable and can be powered with batteries or plugged into an electrical outlet. Patients can use the device at home or work, allowing them to continue their normal daily activities.

The FDA based its approval of the expanded indication of the Optune device on results from a clinical trial involving 695 patients newly diagnosed with GBM that compared those who used Optune with TMZ to those receiving TMZ alone. Patients who used the device along with TMZ lived, on average, about 7 months with no disease progression compared to 4 months for those who had the drug alone. The Optune plus TMZ group survived for an average of 19.4 months after diagnosis compared to 16.6 months for those who were treated with only TMZ. The most common side effect experienced with Optune was skin irritation. Clinical trial participants also experienced a slightly higher incidence of neurological side effects, including convulsions and headaches, compared to subjects receiving TMZ alone. Patients should not use the Optune system if they have an active implanted medical device or a skull defect, have an underlying skin condition involving the scalp or have a known sensitivity to conductive hydrogels, such as those used on electrocardiogram stickers.

The Appellant noted several peer review studies including Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients With Glioblastoma: A Randomized Clinical Trial. Roger Stupp, MD et al JAMA 2017 at 2306-2316.

In the final analysis of this randomized phase 3 trial, the addition of the TT Fields treatment to standard temozolomide maintenance therapy, compared with standard temozolomide maintenance therapy alone, resulted in increased progression-free survival and overall survival in patients with newly diagnosed glioblastoma. After a median follow-up of 40 months, the addition of TT Fields to temozolomide, compared with temozolomide alone, resulted in longer median progression-free survival from the time of randomization, 6.7 months vs

4.0 months and longer median overall survival from randomization, 20.9 months vs 16.0 months, respectively (Exh. 3 CD).

In the appeal at issue the Appellant was diagnosed with new GBM in March 2017. She was treated with surgery, radiation, and chemotherapy. The Appellant experienced significant nausea with the treatments and her physician noted concern regarding myelosuppression and the Appellant's declining white count as well as declining hemoglobin and hematocrit. The Appellant's physician prescribed Optune in July and November 2017. As noted above, the typical course of treatment for GBM is radiation and chemotherapy. However, the Appellant experienced significant complications from chemotherapy and was hospitalized and required blood transfusions. Ms. Miles testified that the Appellant has exceeded average life expectancy for patients with GBM and at present, the Appellant has no other treatment options available.

Based on the arguments and evidence presented, I decline to apply the current LCD to the appeal at issue because the policy is not applicable to the appeal at issue. Specifically, LCD L34823 does not address newly diagnosed GBM. Additionally, I find that the Appellant has submitted ample evidence to support a favorable decision in this appeal based on the peer-reviewed literature, FDA approval, and overwhelming current acceptance in the medical community for the Optune system as a treatment option for recurrent and newly diagnosed glioblastoma.

Conclusion of Law

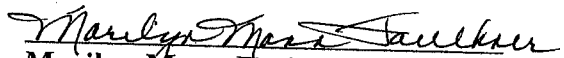
Pursuant to the provisions of Title XVIII of the Act and implementing regulations the Appellant is entitled to Medicare reimbursement for Optune TTFT, billed as electrical stimulation device used for cancer treatment (E0766) and provided to the Appellant on December 25, 2017; January 25, 2018; February 25, 2018; and March 25, 2018.

Order

The decision is **FAVORABLE** for the Appellant. REDACTED The Contractor is ordered to process the claim in accordance with this decision.

SO ORDERED.

Dated: JAN 08 2019


Marilyn Mann Faulkner
U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Irvine, California**

Appeal of:	OMHA Appeal No.: 1-7726450464
Enrollee:	Medicare: Part C
Medicare No.: *****5491A	Before: Marilyn Mann Faulkner U. S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented in the record and at the hearing, a **FULLY FAVORABLE** decision is entered for "Appellant" and "Beneficiary").

Procedural History

This appeal is before the Office of Medicare Hearings and Appeals ("OMHA") following prior adverse determinations made by the Appellant's Medicare Advantage Organization ("MAO"), Humana Health Plan (MAO), and by the Part C Qualified Independent Contractor ("QIC"), MAXIMUS Federal Services. The MAO and the QIC denied the Appellant's request for coverage of proton beam therapy. (Exh. 1.)

OMHA received the Appellant's request for an administrative law judge ("ALJ") hearing on July 30, 2018. (Exh. 4, p. 1.) The Appellant's Request for an ALJ Hearing satisfies the request for hearing timeliness requirement specified in Title 42 Code of Federal Regulations ("C.F.R.") Section 422.602(b). The amount in controversy in this matter exceeds \$160.00 and thus, the amount in controversy in this appeal satisfies the jurisdictional requirement set forth in Title 42 C.F.R. Sections 422.600 and 422.602(d)(1). Accordingly, OMHA has jurisdiction over this case. (C.F.R. §§ 422.602(b); 422.600; 422.602(d)(1).)

A Notice of Hearing was sent to the Appellant, the QIC and Humana Health Plan (the MAO). (Exh. 4, pp. 10-14.) On September 18, 2018, a telephonic hearing was held in this matter in Irvine, California. At the hearing Stephanie Halles, an attorney for Novocure, Julie Miles, RN, and Dan McCoy, case manager, appeared and testified on behalf of the Beneficiary. Dr. Elizabeth Lemaster, MD, and Marsha Taylor, Grievance and Appeals Specialist, appeared and testified on behalf of Humana. The record was held open to allow the Appellant an opportunity to submit additional documentation. The Appellant submitted those documents on October 5, 2018 and they are admitted into the record as Exhibit 5. (Hearing CD).

Issue

Whether Humana Health Plan is required to provide coverage of tumor treatment field therapy (TTFT) for the Beneficiary pursuant to the Medicare Part C provisions of Title XVIII of the Social Security Act and implementing regulations and under the terms of the MAO's Evidence of Coverage.

Findings of Fact

At all times relevant herein, the Appellant/Beneficiary was a member of the MAO and was enrolled in its health plan as of January 1, 2018. (Hearing CD; Exh. 1, p. 10).

The Beneficiary, a 68-year-old male, has a diagnosis of brain cancer (malignant neoplasm of brain unspecified), specifically a glioblastoma multiforme (GMB) brain tumor. According to an evaluation report by Dr. Mark Andersen on February 14, 2018, this cancer was newly diagnosed as a grade IV GBM in January 2018 after pathology from resection of a large right-sided temporal lobe mass on January 12, 2018. Post-operatively, he had a complicated hospital course which included left hemiparesis and was discharge to t rehab facility. The patient underwent radiation and chemotherapy treatment. A post-operative MRI, dated January 18, 2018, was performed to establish a baseline for stability. The MRI revealed suspicious findings for minimal residual tumor to be evaluated on follow-up examinations. (Exh. 2, pp. 3-6).

A subsequent MRI, dated April 25, 2018, stated that the tumor infiltrate had decreased with decreased mass effect. It stated: "Increased size of both solid nodule, peripheral enhancement which is linear and nodular, and cystic components to the right temporal mass highly concerning for tumor progression, Persistent surrounding edema and/or tumor infiltrate has decreased with decreased mass effect.....Midline shift and mass effect has greatly improved from prior MRI." (Exh. 2, pp. 14-16).

Optune tumor treatment field therapy was ordered on April 25, 2018 by Dr. Anderson for the diagnosis of glioblastoma (C71.90). The preferred treatment start date was May 9, 2018. (Exh. 2, pp. 17-18.)

The medical record included treatment and imaging records for the Beneficiary's brain cancer diagnosis which have been summarized above. (Exh. 2).

Following the hearing, the Appellant submitted the Beneficiary's most recent MRI report, dated August 29, 2018, which has been admitted to the record as Exhibit 5, pp. 64-65. The MRI report indicated it was in comparison with the MRI performed on May 21, 2018. The impression was: "Mild interval increase in size of right frontotemporal mass and surrounding tumor infiltrate and/or edema. Slight increase in mass effect and degree of midline shift." (Exh. 5, pp. 64-65).

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. (Social Security Act § 1869(b)(1)(A).)

In implementing this statutory directive, the Secretary has delegated her authority to administer the nationwide hearings and appeals systems for the Medicare program to OMHA. (70 Federal Register 36386, 36387 (June 23, 2005).) The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. (42 C.F.R. § 422.608.) Any party to the hearing who is dissatisfied with the ALJ decision may request that the Medicare Appeals Council review the ALJ's decision. (*Ibid.*)

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a favorable portion of the determination, he or she may notify the parties before the hearing and may consider it an issue at the hearing. (42 C.F.R. § 405.1032(a).)¹

C. Standard of Review

According to 42 C.F.R. Section 405.1000(d), the ALJ conducts a de novo review and issues a decision based on the hearing record.

II. Principles of Law

A. Statutes and Regulations

Section 1833 of the Act requires a claim for Medicare payment to include sufficient documentation to determine whether payment is due and the amount of payment.

Section 1862(a)(1)(A) of the Act provides that Medicare payment may be allowed only for services that are considered reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

The Medicare program is administered through CMS, a component of HHS. CMS contracts with organizations to offer plans under the Medicare Advantage program. (Act § 1857.) The Act provides that an MAO must provide the coverage that would be available to a beneficiary under

¹ The regulations in part 405 of the C.F.R. apply to part 422, unless part 422 provides otherwise. (42 C.F.R. § 422.562(d).)

Parts A and B of the Act (except hospice care) ["basic benefits"] as well as certain additional benefits under specified circumstances. (Act § 1852(a)(1).)

In providing "basic benefits," an MAO must comply with national coverage determinations ("NCD") issued by CMS, "[g]eneral coverage guidelines included in original Medicare manuals and instructions unless superceded by operational policy letters or regulations . . .," and local policy coverage determinations issued by Medicare intermediaries and carriers with jurisdiction for claims in the geographic area.² (42 C.F.R. § 422.101(b).)

Pursuant to Title 42 C.F.R. Section 405.1062(a), an ALJ is not bound by a LCD, but will give substantial deference to a LCD if it is applicable to a particular case. According to Title 42 C.F.R. Section 405.1062(b), if an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. An ALJ decision to disregard such a policy applies only to the specific claim being considered and does not have any precedential effect. (42 C.F.R. § 405.1062(b).)

B. Policy and Guidance

Section 1871(a)(2) of the Social Security Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (LMRPs) or local coverage determinations (LCDs). An ALJ is not bound by an LCD, but must give substantial deference to the policy. 42 C.F.R. § 405.1062.

CGS Administrators' LCD L34823 states the following regarding Tumor Treatment Field Therapy:

Coverage Indications, Limitations, and/or Medical Necessity

...

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

The Policy Article A52711 states the following regarding tumor treatment field therapy:

CODING GUIDELINES

Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers.

This code is inclusive of all associated supplies necessary for the effective use of

² MAOs covering more than one local coverage geographic area may adopt the local policy that is most beneficial to plan enrollees as a uniform policy for all plan enrollees. (42 C.F.R. § 422.101.)

code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

Suppliers should contact the Pricing, Data Analysis and Coding (PDAC) Contractor for guidance on the correct coding of these items.

Pursuant to Title 42 C.F.R. Section 405.1062(a), an ALJ is not bound by a LCD, but will give substantial deference to a LCD if it is applicable to a particular case. According to Title 42 C.F.R. Section 405.1062(b), if an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. An ALJ decision to disregard such a policy applies only to the specific claim being considered and does not have any precedential effect. (42 C.F.R. §405.1062(b).)

C. Evidence of Coverage

An MAO is required to disclose to its enrollees, in clear, accurate, and standardized form, certain information about its available health plans including the service area, benefits, and exclusions from coverage. (See Act § 1852(c); see also 42 C.F.R. § 422.111).

The MAO's Evidence of Coverage ("EOC") provides that the MAO covers items and services consistent with Medicare coverage. (Exh. 1.)

Analysis

At issue in this appeal is whether the Humana Health Plan must approve and provide coverage of the tumor treatment field therapy (E0766) for the treatment of the Beneficiary's brain cancer, specifically glioblastoma multiforme (or "GBM") tumor.

Prior Determinations

The Beneficiary's physician ordered Optune therapy on April 25, 2018. The Health Plan made an initial denial of the request on May 4, 2018. The Health Plan denied the request on the basis that LCD L34823 states the therapy is not medically reasonable and necessary. The denial stated that: "Medicare rule says tumor treatment field therapy will be denied as not reasonable and necessary." (Exh. 1, pp. 14-15.)

The Appellant requested reconsideration of the initial determination on May 16, 2018. The Health Plan upheld its previous denial on May 17, 2018 stating that LCD L34823 states that tumor treatment field therapy is not medically reasonable and necessary and that Medicare considers the treatment to be ineffective. The Health Plan forwarded the appeal to Maximus Federal Services, the QIC, for independent review. (Exh. 2, pp. 10-11).

The QIC issued an unfavorable reconsideration decision on May 18, 2018. It held that the Health Plan was not required to cover the Beneficiary's request for tumor treatment field therapy. The QIC explained in relevant part:

Medicare says tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. Based on this information, we decided that Medicare rules for coverage of tumor treatment field therapy (E0766) have not been met. Therefore, we decided that Humana does not have to pre-approve tumor treatment field therapy (E0766) for V. Magee. (Exh. 1, p. 3.)

Hearing Testimony

At the September 18, 2018 telephonic hearing, Stephanie Halles, attorney for Novocure, argued the case on behalf of the Appellant. She emphasized that unlike the Health Plan, the ALJ is not bound by the LCD and that the ALJ must give deference to LCDs but may deviate based on the particular facts of the case. Ms. Halles argued that in this case, departure from the LCD was warranted due to the particular circumstances in this case. (Hearing CD).

Ms. Miles, Specialist for Novocure and an RN, also testified for the Appellant. Ms. Miles provided the facts of this case with respect to the diagnosis of this rare and highly aggressive tumor. She indicated that there were limited treatment options available for GBM treatment and that treatment consisted of resection, radiation and chemotherapy, and that subsequent complications and recurrence were likely. She provided a summary of the Beneficiary's clinical condition in this case as reflected in the medical documentation in the record (as summarized in the Findings of Fact above). She noted that he was diagnosed with GBM per pathology results of the resection that was performed on January 12, 2018 and noted that he had a negative MGMT result, also referred to as "unmethylated" MGMT promoter status. The MGMT stats refers to a gene mutation that, when absent (i.e., negative MGMT result), has been shown to be associated with reduced responsiveness of the tumor to chemotherapy. (Hearing CD).

Ms. Miles indicated that the Beneficiary had begun the standard of care protocols for newly diagnosed GBM which consisted of concurrent chemotherapy and radiation with Temodar on February 14, 2018 and was completed on April 6, 2018. On April 25, 2018, his physician ordered Optune therapy to treat his GBM. The prescription specified a preferred Optune treatment start date of May 9, 2018, which Ms. Miles indicated was consistent with the NCCN-recommended course of treatment for newly diagnosed GBM, which was to begin Optune with concurrent Temodar approximately one month after completing chemo-radiation with Temodar. (Hearing CD; Exh. 5, pp. 3-5).

She noted that in contrast to the QIC decision, the Optune treatment has been approved by the FDA and is the recommended treatment for the Beneficiary's diagnosis per NCCN guidelines. She noted that Optune therapy had been approved by the FDA in 2011 for the treatment of recurrent GBM and approved in 2015 for the treatment of newly diagnosed GBM. She stated that NCCN guidelines recommend the use of tumor treatment field therapy as a standard of care in patients with newly diagnosed and recurrent GBM. She stated that in this case, the Beneficiary was MGMT negative which was even greater indicator of use of the drug since a negative result had been shown to be associated with reduced responsiveness of the tumor to chemotherapy alone. She argued that given the aggressive nature of the Beneficiary's brain cancer and the lack of other available treatment, tumor treatment field therapy was the best FDA approved option the Beneficiary had at this time. (Hearing CD.)

Ms. Miles indicated that there was broad medical consensus on the effectiveness and benefits of TTFT; and that not only was the treatment included in NCCN's guidelines as a Category 1 recommended treatment for newly diagnosed GBM, over 800 leading oncology centers across the US were certified to prescribe and provide Optune TTFT, which reflects the widespread use and acceptance of the treatment. She further noted that Optune TTFT was covered for uses consistent with its FDA-approved indications under published coverage policies by many commercial insurance companies-including Humana for its commercial (non-Medicare) plan subscribers-as well as a number of state Medicaid programs, further demonstrating broad medical consensus. (Hearing CD.)

Medicare Rules and Policies Regarding Coverage of Tumor Treatment Field Therapy

As indicated above, a Health Plan must pay for a service if Original Medicare would pay for such service. Medicare provides coverage for items and services that are reasonable and necessary to diagnose or treat an illness or condition. CMS has not issued specific coverage criteria in the form of an NCD but the CMS contractor in the local coverage area at issue, CGS Administrators, has issued an LCD regarding TTFT therapy. The LCD states the following: "Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary."

As stated above, and as argued by the Appellant, an ALJ is not bound by a LCD, but will give substantial deference to a LCD if it is applicable to a particular case (Title 42 C.F.R. Section 405.1062(a). According to Title 42 C.F.R. Section 405.1062(b), if an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. An ALJ decision to disregard such a policy applies only to the specific claim being considered and does not have any precedential effect. (42 C.F.R. §405.1062(b).)

FDA Approval of Optune TTFT Therapy

Per FDA documentation submitted by the Appellant and the FDA website, Optune therapy is FDA-approved for recurrent and newly diagnosed glioblastoma multiforme (GBM) brain tumors. Optune was FDA-approved through FDA premarket approval process (PMA) in April 2011 for patients diagnosed with recurrent glioblastoma. As indicated by the Appellant, Optune was approved through the PMA pathway, which is the most stringent pathway for approval of devices and that only 2% of medical devices are approved through the PMA pathway. The FDA described the PMA pathway stating: "OMA approval is based on a determination by FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s)."³

In October 2015, the FDA approved Optune for treatment of newly diagnosed GBM. The approval was based on the results of a randomized controlled trial (called EF-14 Trial) of 695 patients comparing Optune plus temozolomide to temozolomide alone in patients with newly diagnosed GBM. (See Exh. 5, pp. 10-18).

³ FDA, <https://www.fda.gov/MedicalDevicesDeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm>

NCCN Guidelines

Optune is included in the National Comprehensive Cancer Network (NCCN) guidelines with a Category 2B consensus recommendation for recurrent glioblastoma and a Category 1 recommendation, which reflects uniform consensus based on high level of evidence, for newly diagnosed GBM in combination with temozolomide. (Exh. 5, pp. 19-23).

Peer-Reviewed Literature Submitted by the Appellant

Journal of the American Medical Association (JAMA) (Published December 15, 2015): Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma.

The article published the interim results of the EF-14 Trial, as mentioned above under the FDA approval. The results showed superior efficacy both in progression-free survival as well as overall survival. According to the literature, significantly, the EF-14 trial was the first trial in more than a decade to demonstrate statistically and clinically significant extension of overall survival in patients with newly diagnosed GBM regardless of patient characteristics. The interim data of EF-14 trial showed the following:

- Patients treated with TTFT together with temozolomide demonstrated a significant increase in progression free survival compared to temozolomide alone
- Patient treated with TTFT together with temozolomide also demonstrated a significant increase in overall survival compared to temozolomide alone
- The percentage of patient alive at 2 years in the TTFT together with temozolomide arm was 43% compared to 29% in the temozolomide alone arm.

(Exh. 5, pp. 24-32).

The Journal of the American Medical Association (Published December 19, 2017): Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients with Glioblastoma.

The final analysis of the EF-14 trial was published in JAMA in December 2017 and showed that the overall survival and progression free survival were each significantly extended by 37% for patients who received Optune plus temozolomide compared to patient who received temozolomide alone. The analysis demonstrated a greater than one in eight chance of 5 year survival for patients with newly diagnosed GBM treated with Optune and temozolomide. The statistically significant benefit of Optune with temozolomide on overall survival was seen in all pre-specified patient subgroups, regardless of prognostic factors such as age, performance status, MGMT promotor methylation and extent of resection.

The article indicated that patients treated with Optune plus temozolomide experienced overall survival of 20.9 months versus 16 months for patients treated with temozolomide alone. The 5-year survival rate increased from 5% to 13% for patients with Optune with temozolomide versus patient treated with temozolomide alone. There was no increase in systemic adverse events from Optune plus temozolomide versus temozoloide alone.

(Exh. 5, pp. 33-43).

Based on the Evidence in the Record, I find that Tumor Treatment Field Therapy for Treatment of the Beneficiary's Glioblastoma Multiforme Brain Cancer is Medically Reasonable and Necessary per Medicare Rules and Policy

In this case, the record shows that the Beneficiary was recently diagnosed with brain cancer, specifically glioblastoma multiforme or "GBM," a rare and highly aggressive cancer. Following standard of care protocol of treatment that consisted of a combination of chemotherapy and radiation with Temodar, the Beneficiary's physician, Dr. Anderson, ordered tumor treatment field therapy in combination with Temozolomide (or Temodar).

In the letter from Dr. Anderson dated May 7, 2018, he indicated that tumor treatment field therapy should be approved for this Beneficiary as it was the standard of treatment for patients with newly diagnosed and recurrent GBM and that NCCN guidelines had been updated in 2015 to include TTFT treatment for such individuals. Dr. Anderson explained that following the Beneficiary's course of chemotherapy and radiation treatment, TTFT was the best FDA approved treatment option at this time for treating his GBM. Dr. Anderson concluded that, "Optune is the only promising option for him at the present time" and that based on his orphan disease status, limited treatment options and the favorable outcomes and higher quality of life afforded with this treatment, TTFT should be covered for the Beneficiary. (See Exh. 1, pp. 24-26).

Based on the peer-reviewed articles, NCCN guidelines, medical literature and arguments presented in the record and at the hearing, it is clear that TTFT for patients with recurrent and newly diagnosed GBM is the standard of care protocol following resection and combination of chemotherapy and radiation treatment. As stated above, the FDA approved TTFT treatment for patients with recurrent GBM in 2011, and then later approved TTFT treatment for patient with newly diagnosed GBM in 2015. The FDA approvals were based on large randomized trials which had shown proven results of the effectiveness of TTFT. These trials are further discussed and widely accepted as treatment for GBM, as published in the Journal of American Medical Association in both 2015 and in 2017 (See above for the summary). TTFT has also been included as the stand of care in appropriate individuals in the NCCN Clinical Practice Guidelines that were updated in 2015. The NCCN guidelines provide a Category 2B consensus recommendation for TTFT treatment for recurrent GBM and a Category 1 recommendation for TTFT treatment for newly diagnosed GBM concurrent with temozolomide. A Category 1 NCCN recommendation reflects *uniform consensus based on high level of evidence*. Furthermore, more than 800 leading oncology centers across the U.S. are certified to prescribe and provide Optune TTFT, reflecting widespread use and acceptance by relevant experts and specialists nationwide. It is also interesting to note that Optune TTFT has been covered for uses consistent with FDA-approved indications under published coverage policies by many commercial insurance companies-including Humana for its commercial (non-Medicare) plan subscribers-as well as a number of state Medicaid programs, all of which further demonstrates broad medical consensus.

Based on the above, I find that the use of tumor treatment field therapy for the treatment of the Beneficiary's GBM brain tumor is medically reasonable and necessary. As indicated by Dr. Anderson, the Beneficiary's treatment options are limited and TTFT has been proven to be effective for the Beneficiary's clinical condition. With use of TTFT, in combination with

temozolomide, the data and medical consensus shows that the Beneficiary would be provided a greater quality of life as well as increased survival rate. In this case, given the aggressive nature of the GBM tumor, it appears from all the literature that TTFT is the Beneficiary's most promising FDA-approved treatment option available to him and that this treatment option has been widely accepted as the standard of treatment in patients with recurrent and newly diagnosed GBM.

Thus, I find that the Appellant's coverage request for tumor treatment field therapy for the treatment of GBM brain cancer is medically reasonable and necessary in this case. I have taken into account the applicable LCD and have declined to follow it in this case for the extensive reasons I have outlined above.

Conclusions of Law

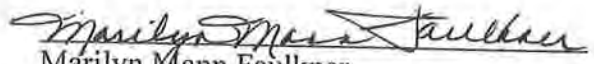
The Health Plan is required to provide coverage for tumor treatment field therapy for the treatment of the Beneficiary's glioblastoma multiforme (GBM) brain tumor cancer pursuant to the Medicare Part C provisions of Title XVIII of the Social Security Act and implementing regulations and policies and under the terms of the Health Plan's Evidence of Coverage.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated: OCT 30 2018


Marilyn Mann Faulkner
U. S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of: [REDACTED]	Member #: FM000244800
Beneficiary: [REDACTED]	ALJ Appeal No.: 1-8088112646
Medicare #: *TU49	Before: Lissette M. Figueroa U.S. Administrative Law Judge
Medicare Advantage Organization (MA): FirstCarolinaCare Insurance Company	

DECISION
FULLY FAVORABLE

After careful consideration of the evidence in the record and the arguments presented at the hearing, a FULLY FAVORABLE decision is entered for [REDACTED] ("Appellant").

Procedural History

This case is before the undersigned Administrative Law Judge ("ALJ") upon a timely request for hearing filed by Appellant's appointed representative following prior determinations made by FirstCarolinaCare Insurance Company ("FirstMedicare Direct"), his Medicare Advantage ("MA") organization and Maximus Federal Services ("Maximus"), the Medicare Part C QIC, an independent review entity.

On May 21, 2018, Appellant's treating physician, Dr. Simon Khagi, prescribed the Optune system for Appellant for a diagnosis of C71.9 (malignant neoplasm of brain, unspecified). (Ex. 1, pages 60-62).

On October 31, 2018, FirstMedicare Direct denied Appellant's request because electric stimulation cancer treatment is not a Medicare covered service in accordance with LCD L34823. (Ex. 1, pages 22-26, 51-54). FirstMedicare Direct indicated that there had been no changes to the LCD since their initial denial so Appellant's second request was also denied. (*Id.*) FirstMedicare Direct indicated that initial denial was upheld on May 29, 2018, Maximus issued an unfavorable decision on August 2, 2018, and an ALJ issued an unfavorable decision upholding the denials on October 16, 2018. (*Id.*) On November 2, 2018, Novocure, the manufacturer of the device requested an expedited appeal (Ex. 1, pages 47-49).

On November 2, 2018, FirstMedicare Direct issued an unfavorable redetermination upholding its initial decision to deny coverage for Appellant's second request of an E0766 electrical stimulation cancer treatment. (Ex. 1, pages 14-20).

In a November 6, 2018 unfavorable reconsideration decision, Maximus agreed with FirstMedicare Direct that it does not have to pre-approve tumor treatment field therapy ("TTFT") because Medicare rules says tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. (Ex. 1, pages 8-13). Maximus cites Local Coverage Determination for Tumor Treatment Field Therapy (TTFT) (LCD L34823) (effective 1/1/17).

Appellant, through his appointed representative, filed a request for an ALJ hearing that was received by the Office of Medicare Hearings and Appeals ("OMHA") on November 9, 2018. (Ex. 3). On December 18, 2018, Appellant's counsel submitted a pre-hearing brief with four attachments. (Ex. 5, pages 1-9). On January 7, 2019 FirstMedicare Direct's counsel submitted an October 16, 2018 ALJ decision by Judge Goga and LCD L34823. (Ex. 5, pages 10-20).

The telephone hearing was conducted on Tuesday, January 8, 2019. (Ex. 4). Appellant was represented at the hearing by Counsel, Debra Parrish, Esq. (*Id*; Hearing CD). Julie Miles participated as Appellant's witness. (*Id*). Counsel, Joe Carruthers, Esq., represented FirstMedicare Direct. (*Id*). Holly Weiss, RN; Sharon Taylor, RN; and Erin Heckethorn, Director of Compliance, also appeared for FirstMedicare Direct. (*Id*).

Ms. Taylor explained that Appellant first requested preauthorization on May 29, 2018, which was denied that same day. (Hearing CD). On July 26, 2018, FirstMedicare Direct received an urgent appeal request with coverage denied that same day and on August 2, 2018 Maximus affirmed the denial. (*Id*). On October 30, 2018, FirstMedicare Direct received another prior authorization request which was denied and the denial was upheld at the first two levels of the appeals process. (*Id*).

After a thorough review of the record and the arguments presented at the hearing, the ALJ concludes that the E0766 electrical stimulation cancer treatment requested by Appellant does meet Medicare's coverage criteria and as a result, FirstMedicare Direct has to authorize this DME item for Appellant.

Issue

The issue to be determined by the ALJ is whether FirstMedicare Direct was correct to deny preauthorization for an Optune device and transducer arrays (HCPCS code E0766) for Appellant pursuant to the Medicare Part C provisions of Title XVIII of the Social Security Act (the "Act").

Findings of Fact

Appellant/enrollee, a 73-year old gentleman, was diagnosed with right temporoparietal glioblastoma (WHO grade IV IDH-wildtype) with subarachnoid involvement on March 15, 2018, after undergoing a resection. (Ex. 1, pages 63-74). Appellant/enrollee complete a short

course of radiation on 5/2/18 and underwent chemotherapy through August 2018. (*Id.*) Appellant's treating physician recommended Optune alternating electric field therapy plus adjuvant temozolomide which is now an NCCN Category 1 recommendation following postoperative standard brain radiation therapy with concurrent temozolomide. (Ex. 1, pages 57-59).

The case file also includes the following relevant documentation:

1. Dr. David Michael Ashley's 8/31/18 progress note. (Ex. 1, pages 63-74).
2. FDA's April 8, 2011 premarket approval application for the NovoTTF-100A System. (Ex. 1, pages 114-118).
3. FDA's October 5, 2015 approval of premarket approval supplement application for the Optune™ (formerly the NovoTTF-100A System). (Ex. 1, pages 110-113).
4. NCCN Clinical Practice Guidelines in Oncology for Central Nervous System Cancers; an article from the Journal of the American Medical Association (JAMA), published online on February 1, 2018, on Influence of Treatment With Tumor-Treating Fields on Health-Related Quality of Life of Patients With Newly Diagnosed Glioblastoma A Secondary Analysis of a Randomized Clinical Trial; an article from JAMA, 2017;318 (23): 2306-2316 on Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs. Maintenance Temozolomide Alone on Survival in Patients with Glioblastoma A Randomized Clinical Trial; an article from JAMA Volume 314, Number 23, pages 2535-2543, December 15, 2015 on Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma A Randomized Clinical Trial (Ex. 1, pages 75-109).
5. Optune information including several articles in medical journals. (Ex. 1, pages 119-272).
6. CD containing 51 favorable ALJ decisions; 51 Optune TTFT medical policies; 18 peer reviewed articles; 11/18/14 FierceBiotech article on trial halted early; 11/27/13 CMS letter awarding HCPCS code; HCPCS decision tree flowchart; Medicare Matters MM8531 – E0766 issuance; July 2018 declaration of Justin Kelly, RN; NCCN guidelines 2013, 2016, 2017, and 2018; July 2018 Novocure list of patents; FDA's April 8, 2011 premarket approval application for the NovoTTF-100A System; FDA's October 5, 2015 approval of premarket approval supplement application for the Optune™ (formerly the NovoTTF-100A System); and March 2, 2018 ASTRO presentation.

Appellant requested an Optune device to treat his brain cancer. (Ex. 1). First Medicare Direct denied Appellant's request, the denial was affirmed by Maximus, and Appellant requested an ALJ hearing. (Ex. 1; Ex. 3).

Legal Framework

I. ALJ Review Authority

A. Scope of Review

Under the implementation policy of the Centers for Medicare and Medicaid Services (“CMS”), a component of the United States Department of Health and Human Services, all Medicare Part C claims, which have been issued a reconsideration by an independent entity, are governed by the ALJ Hearing Procedures outlined in 42 C.F.R. §§ 422.600 et seq.¹

B. Standard of Review

“The [Office of Medicare Hearings and Appeals] directs four field offices staffed with Administrative Law Judges who conduct “de novo” hearings” 70 Fed. Reg. 36386 (June 23, 2005). *See also* In the case of Atlantic Anesthesia Associates, P.C., M.A.C. (June 17, 2004) (“An ALJ qualified and appointed pursuant to the Administrative Procedure Act acts as an independent finder of fact in conducting a hearing pursuant to section 1869 of the Act. This requires *de novo* consideration of the facts and law.”).

II. Legal Authority Binding on ALJs

An ALJ is bound only by statutes enacted by Congress, regulations issued under the Act, rulings issued by CMS, and national coverage decisions in effect during the period at issue.² An ALJ should consider, but is not bound by, any other policy statements, instructions, and guides issued by CMS or by any Local Medical Review Policy. While not binding on the ALJ, however, these manual and policy sections are entitled to substantial deference.³

III. Principles of Law

A. Statutes and Regulations

1. Medicare Part C

The Medicare program, Title XVIII of the Act (42 U.S.C. §§ 1395 – 1395ggg), is administered through CMS. The Secretary of the Department of Health and Human Services is authorized to enter into contracts with private entities for the day-to-day operations of the program.⁴

The Medicare Advantage (“MA”) program (Part C of the Act) provides that a MA organization offering a MA plan must provide enrollees, at a minimum, with all basic Medicare-covered services by furnishing the benefits directly or through arrangements, or by paying for the benefits. MA organizations also may provide mandatory and optional supplemental benefits through their plans.⁵

A MA organization must disclose to each beneficiary enrolling in a MA plan offered by the organization a detailed content of plan description, including, but not limited to, the plan’s

¹ 63 Fed. Reg. 35107, June 26, 1998, as amended at 70 Fed. Reg. 4740, Jan. 28, 2005

² See 42 CFR §§ 401.108 and 405.860

³ *Lyng v. Payne*, 476 U.S. 926, 939 (1986)

⁴ §1842(a)(1)(A) of the Act

⁵ §1852(a) of the Act, 42 CFR §422.100

service area, benefits, access, out-of-area coverage, emergency coverage, premiums and cost-sharing (such as co-payments, deductibles and coinsurance). This information must be offered at the time of enrollment and at least annually after that, in a clear, accurate, and standardized form.⁶

2. Medicare Part B

The Supplementary Medical Insurance program (Part B of the Act) provides coverage for (1) a variety of medical services and supplies furnished by physicians, or by others in connection with physicians' services, (2) for outpatient hospital services, and (3) for a number of other specific health-related items and services including, but not limited to, durable medical equipment ("DME").⁷

DME is defined as equipment which (1) can stand repeated use; (2) is primarily and customarily used to serve a medical purpose; (3) is generally not useful to a person in the absence of illness or injury; and (4) is appropriate for use in the home.⁸

The Act precludes payment for any items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.⁹

B. Policy and Guidelines

1. Local Coverage Determination for Tumor Treatment Field Therapy (TTFT)

(L34823)

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements.

The purpose of a Local Coverage Determination (LCD) is to provide information regarding "reasonable and necessary" criteria based on Social Security Act § 1862(a)(1)(A) provisions.

In addition to the "reasonable and necessary" criteria contained in this LCD there are other payment rules, which are discussed in the following documents, that must also be met prior to Medicare reimbursement:

- The LCD-related Standard Documentation Requirements Article, located at the bottom of this policy under the Related Local Coverage Documents section.

⁶ 42 CFR §422.111

⁷ §§1832(a)(2)(I) and 1861(s)(6) of the Act

⁸ 42 CFR §414.202

⁹ §1862(a)(1)(A) of the Act; 42 U.S.C. §1395y(a)(1)(A)

- The LCD-related Policy Article, located at the bottom of this policy under the Related Local Coverage Documents section.
- Refer to the Supplier Manual for additional information on documentation requirements.
- Refer to the DME MAC web sites for additional bulletin articles and other publications related to this LCD.

For the items addressed in this LCD, the “reasonable and necessary” criteria, based on Social Security Act § 1862(a)(1)(A) provisions, are defined by the following coverage indications, limitations and/or medical necessity.

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

2. Local Coverage Article: Tumor Treatment Field Therapy (TTFT) Policy Article (A52711)

....
Information provided in this policy article relates to determinations other than those based on Social Security Act §1862(a)(1)(A) provisions (i.e. “reasonable and necessary”). Tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act §1861(s)(6)). In order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met. In addition, there are specific statutory payment policy requirements, discussed below, that also must be met.

Code E0766 is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling.

Code A4555 is not valid for billing to Medicare. If code A4555 is billed, it will be denied as an invalid code.

....
CODING GUIDELINES

Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers. This code is inclusive of all associated supplies necessary for the

effective use of code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

Analysis

Mr. Carruthers argued there is no NCD on tumor treatment field therapy ("TTFT"), the applicable LCD indicates this treatment is not covered, the prior ALJ decision was unfavorable. (Hearing CD).

Ms. Parrish argued Judge Goga's decision is wrong as a matter of law and had she been aware of it she would have appealed it. (*Id.*) LCDs are not binding on an ALJ in a Part C appeal, Part C plans must follow Medicare guidance and DME MAC Medical Directors have indicated that LCD L34823 does not apply to newly diagnosed glioblastoma. (*Id.*; Ex. 5, pages 4-9). Therefore, since the LCD does not apply the three part reasonable and necessary analysis would apply: what does the peer review literature say, is there a consensus of experts, and has this treatment been widely accepted by the relevant community. (Hearing CD). The positive results were so overwhelming when they were conducting the clinical trials that they recommended the study be terminated early to allow those patients who were not receiving the treatment to cross over to receive this therapy. (*Id.*) This study was published in JAMA, one of the top five medical journals in the country. (*Id.*)

With regard to the experts' consensus, Ms. Parrish pointed out TTFT has a level 1 recommendation by the NCCN guidelines give a level 1 recommendation for TTFT, which means there is unanimous agreement among the experts that this treatment should be offered to individuals with newly diagnosed glioblastoma. (*Id.*) This treatment is widely accepted and has been prescribed in all 50 states, the District of Columbia, and Puerto Rico. (*Id.*)

Ms. Parrish further argued the plan could not point to LCD L34823 in view of the clarification that has since been issued by the DME MAC Medical Directors indicating the LCD does not apply to patients such as Appellant who have newly diagnosed glioblastoma and the medical standard of care for such a diagnosis. (*Id.*)

Ms. Miles, a registered nurse, testified Appellant was diagnosed with glioblastoma in March of 2018, was treated with radiation and temozolomide (TMZ), and in May 2018 his neuro-oncologist, Dr. Khagi, determined Optune TTFT was the best treatment option for Appellant's glioblastoma. (*Id.*; Ex. 1, pages 57-59). Appellant had been unable to start treatment until he decided to pay out-of-pocket in November of 2018. (Hearing CD). TTFT is the only treatment left for Appellant other than an NHI clinical trial he is trying to see if he qualifies for. (*Id.*)

In response to the ALJ's inquiry regarding whether there had been a final decision from the DME MAC Medical Directors, Ms. Parrish explained they had not met the September 2018 deadline to issue a final decision. (*Id.*) There has been a delay because, in the first week of October 2018, new regulations to revise an LCD were issued which require the Medical

Directors to convene an exterior advisory committee with certain attributes and that infrastructure has not yet been set up. (*Id.*)

Mr. Carruthers argued Appellant was represented by another attorney, Stephanie Hales, Esq., and Ms. Miles was also one of the representatives at ALJ Goga's hearing and that if Judge Goga's unfavorable decision was wrong as a matter of law as Ms. Parrish argues, the remedy should have been a level four appeal rather than a new appeal. (*Id.*) Judge Goga knew he was not bound by the LCD but gave it deference. (*Id.*) Mr. Carruthers stated the undersigned ALJ should also give deference to the LCD and judicial deference to Judge Goga's decision. (*Id.*)

Ms. Taylor pointed out the DME MAC letter states LCD L34823 does not address coverage of newly diagnosed glioblastoma. (*Id.*; Ex. 5, page 8). The letter is in response to a reconsideration request and is not an actual coverage policy so the plan would not change coverage based on this letter. (Hearing CD). No coverage policy bulletins or any other CMS official change in direction guidance have been issued so the plan stands by its decision. (*Id.*)

The Optune™ (formerly the NovoTTF-100A system) device is FDA approved as a treatment for adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme (GBM). Optune™ with temozolomide is indicated for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy. Appellant was newly diagnosed with a right temporoparietal glioblastoma on March 15, 2018, which was surgically removed. (Ex. 1, pages 63-74). Appellant underwent chemotherapy and radiation. (*Id.*) He was prescribed Optune to treat his glioblastoma. (Ex. 1, pages 57-62). Appellant falls squarely within the category of patients for whom the Optune device is FDA approved.

Appellant has submitted documentation confirming that the Optune device received an initial April 2011 FDA pre-market approval and later October 2015 FDA pre-market approval supplement. (Ex. 1, pages 110-118; CD attachment at Exhibit 5).

FDA clearance of a device or service is not synonymous with Medicare coverage.¹⁰ The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational."¹¹ The regulations further clarify that CMS uses FDA categorization "*as a factor*" in making coverage decisions.¹² Thus, under Medicare regulations, the fact that a device, such as the NovoTTF-100A System, may be deemed non-experimental by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage.¹³

Therefore, although the Optune/NovoTTF-100A System received FDA approval or clearance for treatment of newly diagnosed glioblastoma, Appellant/beneficiary's medical condition, such FDA approval/clearance alone does not generally entitle a device to Medicare

¹⁰ *In the Case of Vision Quest Industries, Inc.*, (MAC June 2012).

¹¹ See 42 C.F.R. §405.201(a)(2).

¹² See 42 C.F.R. §405.201(a)(1).

¹³ *In the Case of Vision Quest Industries, Inc.*, (MAC June 2012).

coverage. Accordingly, the undersigned ALJ finds that FDA clearance for the Optune by itself does not establish that the device meets Medicare coverage requirements; i.e., that it has been shown to be a medically reasonable and necessary treatment for treatment of newly diagnosed or recurrent glioblastoma multiforme.

Even though the Optune device is FDA approved, so it is safe and effective for Appellant's diagnosis, Medicare does not consider it reasonable and necessary according to LCD L34823. (Ex. 4, pages 1-16; Ex. 5, pages 16-20). Although ALJs are not bound by LCDs, an ALJ must give substantial deference to LCDs applicable to a particular case.¹⁴ An ALJ must explain the reason for not following such a policy in a specific case.¹⁵ Any decision to disregard a policy "applies only to the specific claim being considered and does not have precedential effect."¹⁶

Appellant also submitted additional studies and literature pertaining to the efficacy of TTFT for indications stated in those FDA approvals, including use of the Optune Device for treatment of recurrent Glioblastoma which has not responded to standard therapy (per the April 2011 FDA approval) and for treatment of newly diagnosed Glioblastoma (per the October 2015 FDA approval supplement). (*Id.*)

Among the peer review literature submitted by Appellant, the December 2015 article from the Journal of the American Medical Association (JAMA) titled Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide Vs. Temozolomide Alone for Glioblastoma — A Randomized Clinical Trial, describes the superior results in progression free survival as well as overall survival of glioblastoma patients using TTFields. (Ex. 1, pages 99-108). The December 2017 JAMA article titled Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients With Glioblastoma A Randomized Clinical Trial, concludes that in the final analysis of a randomized clinical trial of patients with glioblastoma who had received standard radiochemotherapy, the addition of TTFields to maintenance temozolomide chemotherapy vs maintenance temozolomide alone, resulted in statistically significant improvement in progression-free survival and overall survival with the results being consistent with the previous interim analysis. (Ex. 1, pages 88-98). The February 2018 JAMA article titled Influence of Treatment With Tumor-Treating Fields on Health-Related Quality of Life of Patients With Newly Diagnosed Glioblastoma, A Secondary Analysis of a Randomized Clinical Trial, shows the addition of TTFields to standard treatment with temozolomide for patients with glioblastoma results in improved survival without a negative influence on HRQoL except for more itchy skin, an expected consequence from the transducer arrays. (Ex. 1, pages 79-87). These trials show the Optune device was safe, non-investigational and effective and appropriate for Appellant's needs, specifically the treatment of newly discovered glioblastoma.

Additional material submitted by the Beneficiary also shows the use of TTFT is generally accepted by the medical community and covered by major insurers. In the 2018 version of the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, Central Nervous System Cancers guidelines, alternating electric field therapy is a

¹⁴ 42 CFR §405.1062

¹⁵ 42 CFR §405.1062(b)

¹⁶ *Id.*

category 1 treatment option suggested for glioblastoma. (Ex. 1, pages 75-77). A Category 1 of evidence and consensus means that based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.¹⁷ This suggestion was found in a treatment guideline from a national cancer organization, not evidence based on an individual physician treating a single patient in a clinical setting.

Based upon the facts of this case, and giving appropriate deference to the LCD policy guidance, the undersigned ALJ declines to follow the LCD in this case, and instead find that the Optune device will be considered reasonable and necessary as specifically applied to Appellant's diagnosis and treatment regimen. In declining to follow the pertinent LCD, the ALJ has considered the following criteria, as suggested by Medicare manual guidance: (1) whether the device can be expected to make a meaningful contribution to the treatment of the patient's illness or injury or to the improvement of his or her malformed body member; (2) whether the device can be considered a reasonable treatment, considering expense versus therapeutic benefits, comparative cost of feasible alternatives, and whether the device serves the same purpose as other available equipment or alternatives; (3) whether all features of the device are required for treatment of the Beneficiary's condition; and, (4) the period of time the DME will be considered medically necessary, which is generally based on the physician's estimate of the time that his or her patient will need the equipment.¹⁸

Moreover, the LCD, as currently published does not cite any studies, articles or other sources for this determination, or specify any specific diagnoses for which the treatment will be considered as not reasonable and necessary. It makes no distinction between recurrent glioblastoma or newly discovered glioblastoma, and the lack of sources or information on which the determination was based makes it unascertainable.

ALJ Goga's decision is not precedential so the undersigned ALJ declines to follow it. The Medicare Appeals Council ("Council") has issued two unfavorable decisions on the E0766 TTFT.¹⁹ MAC decisions have no precedential value but may serve as a guidepost to disposition of similar cases.²⁰ The ALJ disagrees with the Council's conclusions and declines to follow the Council's decisions that Medicare does not currently cover the Optune/TTFT in view of the overwhelming evidence that it is the standard of care per the NCCN category 1 recommendation, the fact that a large number of commercial plans, such as Aetna, Blue Cross Blue Shield, Humana, Cigna, Kaiser, United Healthcare among others, do cover it for newly diagnosed glioblastoma, the large clinical trial, numerous peer review publications, and over 50 ALJ decisions that have departed from the LCD in cases of beneficiaries with the same diagnosis as Appellant.

¹⁷ NCCN Categories of Evidence and Consensus, *see*

https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx

¹⁸ §110.1(c) - Necessary and Reasonable, Chapter 15, Medicare Benefit Policy Manual, Pub 100-02

¹⁹ *BlueCross BlueShield of North Carolina*, Medicare Appeals Council, Docket #M-15-354, January 4, 2016; *Blue Cross Blue Shield of Western New York*, Medicare Appeals Council, Docket #M-17-6134, March 1, 2018

²⁰ *See 70 Fed. Reg. 11420, 11449* (Mar. 8, 2005); *See also Vidant Medical Center*, Medicare Appeals Council, Docket #M-14-398, March 13, 2014

After a careful and thorough review of Appellant's arguments and the evidence in the record, the undersigned ALJ finds the use of the Optune device for an FDA approved indication can be expected to make a meaningful contribution to the treatment of Appellant's glioblastoma. The undersigned ALJ understands that Medicare often times lags behind other insurers in covering new medical technologies but it is unreasonable to deny Medicare coverage in view of the extensive peer review literature, favorable clinical trials, widespread adoption by other health plans, and NCCN Guidelines support.

Therefore, the ALJ concludes the requested Optune device treatment is safe and effective, not experimental or investigational, and appropriate. Accordingly, the device meets Medicare coverage requirements; i.e., that it has been shown to be a medically reasonable and necessary treatment for treatment of Appellant's diagnosis, newly diagnosed glioblastoma. As a result, FirstMedicare Direct must authorize the treatment for Appellant's glioblastoma with the Optune device and transducer arrays (HCPCS code E0766).

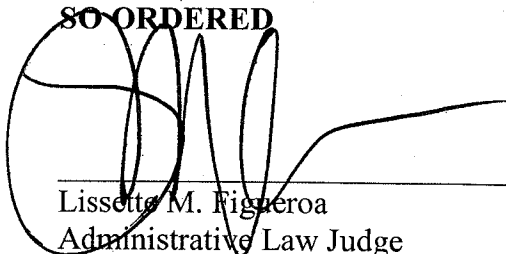
Conclusions of Law

The ALJ concludes that the Optune device and transducer arrays (HCPCS code E0766) requested by Appellant is covered by Medicare so FirstMedicare Direct must authorize/cover this treatment.

Order

Maximus' unfavorable decision is hereby **REVERSED**.

SO ORDERED



Lissette M. Figueroa
Administrative Law Judge

JAN 16 2019

Date



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of:	Redacted through her appointed representative Debra Parrish, Esq.	Qualified Independent Contractor (QIC): C2C Solutions, Inc.
Beneficiary:	Redacted	ALJ Appeal No.: 1-7776963266
HIC No.:	XXX-XX-7474M	Before: Lissette M. Figueroa U.S. Administrative Law Judge
Claim for:	Part B Durable Medical Equipment	

DECISION
FULLY FAVORABLE ON-THE-RECORD

In accordance with Medicare regulations, an Administrative Law Judge (“ALJ”) may issue a fully favorable decision without giving the parties prior notice and without holding a hearing if, the evidence in the record supports such a finding.¹ The ALJ has thoroughly reviewed the record and after carefully analyzing all the documents and arguments contained in the record has reached a fully favorable decision.

Procedural History

Redacted (“Appellant”) is appealing an unfavorable reconsideration decision by C2C Solutions, Inc., the Qualified Independent Contractor (“QIC”), denying coverage for tumor treatment field therapy (“TTFT”) provided to the beneficiary on July 10, August 10, and September 10, 2017.

The supplier, Novocure, Inc., filed claims for reimbursement of the rental of an Optune device and transducer arrays (HCPCS code E0766) for dates of service 7/10/17, 8/10/17, and 9/10/17. (Ex. 1, pages 26-28). Medicare denied payment in 7/18/17, 8/16/17, and 9/15/17 initial determinations. (*Id.*) Novocure, Inc. requested a redetermination. (Ex. 1, pages 14-15).

On November 16, 2017, the Medicare Administrative Contractor (“MAC”) issued an unfavorable redetermination decision denying coverage because based on LCD L34823 TTFT

¹ 42 CFR §405.1038(a)

(E0766) will be denied as not reasonable and necessary. (Ex. 1, pages 12-13). Additionally, the MAC determined that the supplier was responsible for the denied charges. (*Id.*)

On June 15, 2018, the QIC affirmed the denial in an unfavorable reconsideration decision because there is insufficient documentation to quantify the effects of the device. (Ex. 1, pages 1-7). Additionally, the QIC determined that the supplier was responsible for the charges for the denied equipment. (*Id.*)

Appellant's appointed representative and counsel, Debra Parrish, Esq., timely filed a request for an ALJ hearing that was received by the Office of Medicare Hearings and Appeals ("OMHA") on August 6, 2018. (Ex. 3). The ALJ's staff contacted Appellant's counsel to clarify what Appellant had paid for the rental of the Optune device (HCPCS code E0766) since the invoices did not show any paid amount. (Ex. 1, pages 23-25; Ex. 4, pages 1-2). Ms. Parrish explained Appellant had not paid anything yet because the supplier is waiting for the outcome of the appeal. (*Id.*) If the outcome is unfavorable and if Appellant does not have secondary insurance, Novocure will determine if she qualifies for their Patient Access and Reimbursement Assistance Program.² (*Id.*) Novocure billed Medicare \$20,000 per month for the Optune device (HCPCS code E0766). (Ex. 1, pages 23-25). The remaining amount in controversy meets the jurisdictional requirements for a hearing before OMHA.³ Therefore, the jurisdictional predicates are met and the claims for the TTFT (E0766), which are covered by this decision, are properly before the ALJ for *de novo* review.

On August 24, 2018, Debra Parrish, Esq., Appellant's appoint representative and counsel, submitted a pre-hearing brief. (Ex. 4).

After a thorough review of the record, the ALJ finds that the rental of the TTFT device (E0766) met Medicare coverage criteria and documentation requirements, was reasonable and necessary, and is, therefore, covered by Medicare.

Issues

1) Whether the Optune device and transducer arrays (HCPCS code E0766) supplied to Appellant/beneficiary met Medicare's coverage criteria under §§1832(a) and 1861(n) and (s)(6) of Title XVIII of the Social Security Act (the "Act").

2) In the event they do not, whether the waiver of liability provisions of §1879 of the Act apply to Appellant, supplier, or both.

Findings of Fact

The beneficiary, a 74-year old lady, was diagnosed with brain glioblastoma, underwent a craniotomy on 3/15/17, chemotherapy from 4/3/17 through 4/23/17, radiation from 4/4/17 through 4/20/17, and a repeat resection on 5/15/17. (Ex. 2, pages 4-8).

² Optune Patient access and reimbursement assistance, *see* <https://www.optune.com/hcp/ncompass/patient-reimbursement>

³ 67 Fed. Reg. 62478 (October 7, 2002) and 70 Fed. Reg. 11423 (March 8, 2005)

On 7/5/17 Dr. [Redacted] signed Appellant's generated Optune™ prescription form for the beneficiary for a diagnosis of C71.9 (malignant neoplasm of brain, unspecified). (Ex. 2, pages 1-2). The case file also includes the following relevant documents:

1. Optune Service Agreement, Instructions for Use, Product Dossier. (Ex. 1, pages 29-117).
2. NCCN Clinical Practice Guidelines in Oncology for Central Nervous System Cancers. (Ex. 1, pages 118-121).
3. FDA's April 8, 2011 premarket approval application for the NovoTTF™-100A System. (Ex. 1, page 22).
4. CMS' July 26, 2013 letter indicating the NovoTTF™-100A System falls within the DME benefit category. (Ex. 1, page 16).
5. Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma A Randomized Clinical Trial, Journal of the American Medical Association, Volume 314, Number 23, December 15, 2015. (Ex. 1, pages 122-132).
6. Tumor treating fields: concept, evidence and future, Informa healthcare article. (Ex. 1, pages 190-197).
7. NovoTTF-100A: a new treatment modality for recurrent glioblastoma, Expert reviews 2012 article. (Ex. 1, pages 179-189).
8. Chemotherapeutic treatment efficacy and sensitivity are increased by adjuvant alternating electric fields (TTFields), BioMed Central Medical Physics, January 2009. (Ex. 1, pages 166-178).
9. TTFields alone and in combination with chemotherapeutic agents effectively reduce the viability of MDR cell sub-lines that over-express ABC transporters, BioMed Central Cancer, 2010. (Ex. 1, pages 159-165).
10. Disruption of Cancer Cell Replication by Alternating Electric Fields article. (Ex. 1, pages 145-152).
11. Alternating electric fields arrest cell proliferation in animal tumor models and human brain tumors, PMAS article, June 12, 2007. (Ex. 1, pages 153-158).
12. NovoTTF-100A versus physician's choice chemotherapy in recurrent glioblastoma: a randomized phase III trial of a novel treatment modality, Science Direct 2012 article. (Ex. 1, pages 134-144).
13. Interim Analysis of the ER-14 Trial: A Prospective, Multi-center Trial of NovoTTF-100A Together With Temozolomide Compared to Temozolomide Alone in Patients with Newly Diagnosed GBM, Society for Neuro-Oncology, 2014 abstract. (Ex. 1, page 133).
14. CD containing clinical studies, NCCN guidelines, payer policies, FDA approval, statement of adoption, article on clinical trial being stopped, list of patents, prior favorable ALJ decisions.

Appellant seeks coverage for the rental of a TTFT-100A (HCPCS code E0766) for treatment of glioblastoma for dates of service July 10 through September 10, 2017. (Ex. 3). This device is relatively new to cancer treatment.⁴ The first FDA approval, on April 8, 2011, was for

⁴ The Evolving Role of Tumor Treating Fields in Managing Glioblastoma, Guide for Oncologists, American Journal of Clinical Oncology, February 2018, 41(2): 191-196, see <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5779316/>

recurrent GBM, while the most recent October 5, 2015 FDA approval in combination with temozolomide for the treatment of newly diagnosed GBM.⁵

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (“HHS”), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner.⁶

In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA.⁷ The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council.⁸

A hearing before an ALJ is only available if the remaining amount in controversy is \$160 or more.⁹ The request for hearing is timely if filed within sixty days after receipt of the notice of the QIC’s reconsideration decision.¹⁰

B. Scope of Review

Under the Centers for Medicare and Medicaid Services’ (CMS) implementation policy for the Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 (BIPA), Pub. Law 106-554, app. F, 114 Stat. 2763, 2763A-463, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), Pub. Law 108-173, 117 Stat. 2066, all initial determinations by CMS-contracted carriers prior to January 1, 2006, are governed by the ALJ hearing procedures set forth at 20 C.F.R. §§ 404.929 through 404.961 and 42 C.F.R. § 405.855.¹¹

“The issues before the administrative law judge include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in [the appellant’s] favor. However, if evidence presented before or during the hearing causes the administrative law

⁵ FDA, Optune (Formerly the NOVOTTF-100A system) Premarket Approval *see* <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P100034S013>

⁶ Social Security Act (Act) § 1869(b)(1)(A)

⁷ *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005)

⁸ *Id*

⁹ *See* CMS Rul. 02-1, 67 Fed. Reg. 62478, 62480 (Oct. 7, 2002); 70 Fed. Reg. 11420, 11423 (Mar. 8, 2005); 72 Fed. Reg. 73348 (Dec. 27, 2007); 77 Fed. Reg. 59618-59619 (September 28, 2012); 78 Fed. Reg. 59702-59704 (September 27, 2013); 82 Fed. Reg. 45592 (Sep. 29, 2017)

¹⁰ 42 C.F.R. § 405.1002(a)

¹¹ *See* 70 Fed. Reg. 11420, 11424-26 (Mar. 8, 2005)

judge to question a fully favorable determination, he or she will notify [the appellant] and will consider it an issue at the hearing.”¹²

“The administrative law judge may decide a case on the record and not conduct an oral hearing if [the appellant] and all the parties indicate in writing that [they] do not wish to appear before the administrative law judge at an oral hearing.”¹³

C. Standard of Review

The Office of Medicare Hearings and Appeals is staffed with Administrative Law Judges who are qualified and appointed pursuant to the Administrative Procedure Act. They act as independent finders of fact in conducting hearings pursuant to §1869 of the Act. ALJs conduct ‘de novo’ hearings of the facts and law. *See* 70 Fed. Reg. 36386 (June 23, 2005).

II. Legal Authority Binding on ALJs

An ALJ is bound only by statutes enacted by Congress, regulations issued under the Act, rulings issued by CMS, and national coverage decisions in effect during the period at issue.¹⁴ An ALJ should consider, but is not bound by, any other policy statements, instructions, and guides issued by CMS or by any Local Medical Review Policy.¹⁵ While not binding on the ALJ, however, these manual and policy sections are entitled to substantial deference.¹⁶

III. Principles of Law

A. Statutes and Regulations

1. Medicare Part B

The Medicare program, Title XVIII of the Act,¹⁷ is administered through the Centers for Medicare and Medicaid Services (“CMS”), a component of the United States Department of Health and Human Services (“HHS”). Under the Act, the Secretary of the Department of HHS is authorized to enter into contracts with private entities for the day-to-day operations of the program.¹⁸ The entities that contract to administer payment for durable medical equipment are called Durable Medical Equipment Regional Carriers (“DMERCs”). The designated DMERC for the services at issue here is Noridian Healthcare Solutions, DME MAC Jurisdiction D.

The Supplementary Medical Insurance program (Part B of the Act) provides coverage for (1) a variety of medical services and supplies furnished by physicians, or by others in connection with physicians’ services, (2) for outpatient hospital services, and (3) for a number of other

¹² 20 C.F.R. § 404.946(a)

¹³ 20 C.F.R. § 404.948(b)(i)

¹⁴ 42 CFR §405.1060

¹⁵ 42 CFR §405.1062

¹⁶ *Id.*; *Lyng v. Payne*, 476 U.S. 926, 939 (1986).

¹⁷ 42 U.S.C. §§ 1395 – 1395ggg

¹⁸ §1842(a)(1)(A) of the Act

specific health-related items and services including, but not limited to, durable medical equipment ("DME").¹⁹

DME is defined as equipment which (1) can stand repeated use; (2) is primarily and customarily used to serve a medical purpose; (3) is generally not useful to a person in the absence of illness or injury; and (4) is appropriate for use in the home.²⁰

The Act precludes payment for any items or services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.²¹

Additionally, one of the conditions for Medicare payment is that the provider must furnish to the intermediary sufficient information to determine whether payment is due.²²

In the event the services at issue are found to be "not medically reasonable and necessary," section 1879 (a) of the Act provides for waiver of liability of Medicare payments. This section applies only to a denial by reason of "not medically reasonable and necessary," and when:

- (1) The item or service was furnished under assignment; and
- (2) Neither the beneficiary, nor the provider/supplier knew or reasonably could have been expected to know that such services would be excluded from Medicare coverage.

B. Policy and Guidance

1. Local Coverage Determination for Tumor Treatment Field Therapy (TTFT) (L34823) effective 1/1/17 through the present

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements.

The purpose of a Local Coverage Determination (LCD) is to provide information regarding "reasonable and necessary" criteria based on Social Security Act § 1862(a)(1)(A) provisions.

In addition to the "reasonable and necessary" criteria contained in this LCD there are other payment rules, which are discussed in the following documents, that must also be met prior to Medicare reimbursement:

¹⁹ §1832(a) and (2)(B) of the Act; §1861(n) and (s)(6) of the Act

²⁰ 42 CFR §414.202

²¹ §1862(a)(1)(A) of the Act; 42 U.S.C. §1395y(a)(1)(A)

²² 42 CFR §424.5(a)(6)

- The LCD-related Standard Documentation Requirements Article, located at the bottom of this policy under the Related Local Coverage Documents section.
- The LCD-related Policy Article, located at the bottom of this policy under the Related Local Coverage Documents section.
- Refer to the Supplier Manual for additional information on documentation requirements.
- Refer to the DME MAC web sites for additional bulletin articles and other publications related to this LCD.

For the items addressed in this LCD, the “reasonable and necessary” criteria, based on Social Security Act § 1862(a)(1)(A) provisions, are defined by the following coverage indications, limitations and/or medical necessity.

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

2. Local Coverage Article: Tumor Treatment Field Therapy (TTFT) Policy Article (A52711)

Information provided in this policy article relates to determinations other than those based on Social Security Act §1862(a)(1)(A) provisions (i.e. “reasonable and necessary”). Tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act §1861(s)(6)). In order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met. In addition, there are specific statutory payment policy requirements, discussed below, that also must be met.

Code E0766 is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Separate billing of supplies and/or accessories will be denied as unbundling.

Code A4555 is not valid for billing to Medicare. If code A4555 is billed, it will be denied as an invalid code.

CODING GUIDELINES

Code E0766 describes devices that generate electromagnetic fields

utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers.

This code is inclusive of all associated supplies necessary for the effective use of code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

Analysis

The MAC denied coverage because LCD L34823 states TTFT (E0766) will be denied as not reasonable and necessary. (Ex. 1, pages 12-13). The QIC affirmed the denial because there is insufficient documentation to quantify the effects of the device. (Ex. 1, pages 1-7). Appellant argues exact quantification of effectiveness of a treatment is not a requirement for Medicare coverage. (Ex. 3). The undersigned ALJ agrees with Appellant's argument.

CMS has determined the TTFT Optune device (E0766) meets the definition of DME. (Ex. 1, page 16).²³ The supplier has submitted documentation confirming that the Optune device received an initial April 2011 FDA pre-market approval and later October 2015 FDA pre-market approval supplement. Appellant submitted additional studies and literature pertaining to the efficacy of tumor treating fields therapy for indications stated in those FDA approvals, including use of the Optune Device for treatment of recurrent Glioblastoma which has not responded to standard therapy (per the April 2011 FDA approval) and for treatment of newly diagnosed Glioblastoma (per the October 2015 FDA approval supplement). (Ex. 1; CD). Optune is FDA approved for both recurrent and newly diagnosed glioblastoma.

The TTFT Optune device (E0766) is a portable, wearable medical device that produces alternating electrical fields, tumor treating field ("TTFields") within the brain by means of electrically insulated surface transducer arrays placed on the scalp. (Ex. 1, page 87). The TTFields disrupt the rapid cell division exhibited by cancer cells supporting tumor growth inhibition without damage to normal neuronal function or structure or any systemic toxicity. (*Id.*; Ex 1. Page 93).

The applicable LCD in this instance, LCD L34823, titled "Tumor Treatment Field Therapy (TTFT)" states "[t]umor treatment field therapy (E0766) will be denied as not reasonable and necessary" without further explanation. Although pursuant to Medicare regulations an ALJ must give substantial deference to Medicare policy guidance, including applicable LCDs, an ALJ is not required to follow such policy guidance upon providing an explanation in the decision as to the reasons why the policy will not be followed.²⁴

LCD L34823 does not articulate the reason the contractor has determined categorically that the device is not reasonable and necessary. The LCD does not list any supporting materials such as clinical trials and peer review journal articles used to reach the determination that TTFT

²³ Local Coverage Article: Tumor Treatment Field Therapy (TTFT) Policy Article (A52711)

²⁴ 42 CFR §405.1062

is not reasonable and necessary. A January 4, 2016 Departmental Appeal's Board's Medicare Appeal Council unfavorable decision on TTFT is distinguishable because the applicable LCD in that case did include a list of sources on which the non-coverage determination was based.²⁵ In this instance, LCD L34823 does not include any such materials, sources, or references to deduce what the determination was based on.

The 2015 FDA approval of TTFields for newly diagnosed glioblastoma was based on the results of a randomized, phase 3 controlled clinical trial of 695 patients that compared Optune with temozolomide (TMZ), a chemotherapy drug, versus TMZ alone. (Ex. 1, pages 123-133). The trial was done between July 2009 and November 2014. (Ex. 1, page 126). The results of the clinical trial were published in the December 15, 2015 Journal of the American Medical Association. (Ex. 1, pages 123-133). This trial (EF-14) showed superior efficacy both in progression free survival and overall survival. (*Id.*) Patients who received TTFields plus temozolomide had a median overall survival of 20.5 months compared with 15.6 month in those who received temozolomide alone. This was the first trial in more than a decade to demonstrate a significant extension of overall survival in patients with newly diagnosed glioblastoma regardless of any other patient characteristics. (*Id.*)

The trial met its primary and main secondary endpoints and was closed to accrual after the interim analysis because it showed adjuvant temozolomide chemotherapy and NovoTTF provided a clinically and statistically significant improvement in progression-free and overall survival. (Ex. 1, pages 126, 128-129, 133). Of special significance, based on the results of the interim analysis, the trial's independent data and safety monitoring committee recommended termination of the trial to allow patients in the control group to cross over to receive TTFields. (*Id.*) The FDA approved the study termination so the trial was closed to recruitment on November 29, 2014. (Ex. 1, page 126). The final analysis of this randomized clinical trial was published in the December 29, 2017 Journal of the American Medical Association (JAMA).²⁶ It concluded that in patients with glioblastoma who had received standard radiochemotherapy, the addition of TTFields to maintenance temozolomide chemotherapy vs maintenance temozolomide alone, resulted in statistically significant improvement in progression-free survival and overall survival.²⁷ The results were consistent with the previous interim analysis²⁸.

Additionally, the case file contains a 7/9/13 redacted letter from Maximus, the Part C QIC, indicating it agreed with the appellant that the Part C plan, Anthem Blue Cross Life and Health Insurance Company, had to pre-approve the NovoTTF100-A System (the previous name of the Optune device). (Ex. 1, pages 20-21).

Appellant further argues that based on the strength of the peer-reviewed literature and the lack of medical alternatives the Optune device has been certified at more than 800 cancer treatment centers and is covered by virtually every major payer in the United States, including,

²⁵ In the case of BlueCross BlueShield of North Carolina, M-15-1354

²⁶ Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients With Glioblastoma A Randomized Clinical Trial, JAMA, 12/19/17, *see* <https://jamanetwork.com/journals/jama/fullarticle/2666504>

²⁷ *Id.*

²⁸ *Id.*

but not limited to, Highmark, Aetna, Anthem, Humana, Kaiser, United HealthCare, Cigna, Geisingers, and several Blue Cross plans.

LCD L34823 is arbitrary and the undersigned ALJ declines to follow it in the face of overwhelming evidence that TTFT is a medically reasonable and necessary part of Appellant's treatment plan. TTFT is becoming the standard of care for treating glioblastoma as evidenced by the submitted peer-reviewed literature, NCCN Guidelines for Anaplastic Gliomas/Glioblastoma for 2017 and 2018 category of evidence 2A (based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate), the Mayo Clinic's information on Glioblastoma, and the fact that numerous commercial insurers cover the treatment.²⁹ (list of commercial insurers that cover TTFT in CD).

After a careful and thorough review of Appellant's arguments and the evidence in the record, the undersigned ALJ finds that the use of the Optune device for an FDA approved indication can be expected to make a meaningful contribution to the treatment of Appellant's glioblastoma. Moreover, such use of the Optune device has been shown to improve survival rates over other available therapies. The device is, therefore, reasonable and necessary for the treatment of Appellant's glioblastoma. Medicare always lags behind other insurers in covering new medical technologies but it is unreasonable to deny Medicare coverage in view of the extensive literature, favorable clinical trials, widespread adoption by other health plans, and NCCN Guidelines support.

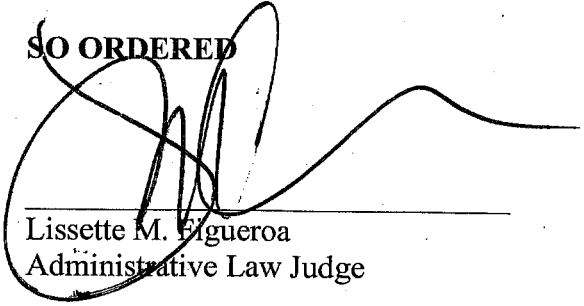
Conclusions of Law

The TTFT (E0766) met Medicare coverage criteria and documentation requirements, was reasonable and necessary, and is, therefore, covered by Medicare.

Order

The QIC's decision is hereby **REVERSED** and the Medicare contractor is **DIRECTED** to process the claims in accordance with this decision.

SO ORDERED


Lissette M. Figueroa
Administrative Law Judge

AUG 31 2018

Date

²⁹ Glioblastoma, Mayo Clinic, *see* <https://www.mayoclinic.org/diseases-conditions/glioblastoma/cdc-20350148>



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami Field Office**

Appeal of:	ALJ Appeal No.: 1-7835293187
Beneficiary:	Medicare Part B
HICN:	Before: Lisette M. Figueroa U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record and at the hearing, a **FAVORABLE** decision is entered in the appeal of (Appellant).

Procedural History

Appellant submitted claims to Medicare for an E0766 (electrical stimulation device used cancer treatment) for the dates of services of September 19, 2017, October 19, 2017, November 19, 2017, and December 19, 2017. The claims were initially denied on September 25, 2017, because Medicare guidelines were not met. Redetermination request was made to CGS, the Medicare Contractor with jurisdiction. On January 29, 2018, CGS concluded the following:

Tumor treatment field therapy (E0766) or therapy supplies (A4555) is not covered by Medicare as the currently published studies in the medical literature do not clearly document the effectiveness of this device per LCD L34823. (Exhibit 1, pages 13-15).

Appellant requested a reconsideration review by the Qualified Independent Contractor (QIC) and on August 14, 2018, the QIC affirmed the Plan. (Exhibit 1, pages 1-7). The QIC stated the medical documentation did not support the need for the device. In addition, the QIC stated no medical records were submitted to explain why this particular Beneficiary should be considered for this treatment which is required per LCD L34823. Lastly, the QIC held Novocure liable for the claims at issue. (Exhibit 1, page 4).

On August 27, 2018, the Office of Medicare Hearings and Appeals (OMHA) received the Appellant's timely Request for Medicare Hearing by an Administrative Law Judge (ALJ) from the Beneficiary's representative. (Exhibit 3, page 1). The remaining amount in controversy meets the jurisdictional

¹ Enrollee's Representative is Debra Parrish of the Parrish Law Offices

requirements for a hearing before OMHA.² Therefore, the jurisdictional predicates are met and the claim for ambulance services which is covered by this decision is properly before the ALJ for *de novo* review.

Within the Request for Hearing, Attorney Parrish requested pending dates of service at issue be consolidated to the hearing. (Exhibit 3, page 2). Dates included May 19, 2016 – July 19, 2016; August 19, 2016 – October 19, 2016; November 19, 2016 – January 19, 2017; February 19, 2017 – April 19, 2017; and May 19, 2017 – August 19, 2017. Upon review, the undersigned determined Novocure had already filed a Request for Hearing for the requested dates and despite my best efforts to consolidate the dates, I was unable to add the pending dates to the hearing based upon communication with OMHA HQ and Central Operations.

On October 30, 2018, the undersigned conducted a telephone hearing from the OMHA Miami Field Office. The QIC was provided with a notice of hearing, but did not attend. Attendees at the hearing included: Debra Parrish, Counsel for the Beneficiary, Mr. Julie Miles, RN and Dan McCoy, Manager on behalf of Novocure. During the hearing, it was determined records were missing; therefore, Ms. Parrish was provided with a deadline (November 9, 2018) to send the additional records. Same was received and admitted into the record as Exhibit 5. The record includes Exhibits 1-4 and the recorded hearing testimony.

Issues

- 1) Whether payment can be made under Part B of the Medicare program for the E0766 (electrical stimulation device used cancer treatment) device provided to the Beneficiary on September 19, 2017, October 19, 2017, November 19, 2017, and December 19, 2017, and whether the item was medically reasonable and necessary pursuant to the provisions of Section 1862 (a)(a) of the Social Security Act and 42 C.F.R. § 411.15 (k).
- 2) Whether payment can otherwise be made to the Appellant pursuant to the waiver of liability provisions under Section 1879 of the Act and 42 C.F.R. § 411.406, if it is determined that the item was not medically reasonable and necessary under Section 1862 (a)(1) of the Act.

Findings of Fact

1. Optune Prescription Form dated April 7, 2016, indicated the physician ordered a 6-month prescription for the Beneficiary due to malignant neoplasm of the frontal lobe. (Exhibit 2, page 9).
2. Optune Service Agreement and delivery confirmation was signed by the Beneficiary on May 19, 2016. (Exhibit 1, pages 40-53).
3. Life Threatening Condition- Letter of Medical Necessity dated September 30, 2016, was written by Dr. MD to request authorization for Optune treatment. (Exhibit 1, pages 20-22). Assessment of Need was completed on April 9, 2016. (Exhibit 1, page 23).

² 67 Fed. Reg. 62478 (October 7, 2002) and 70 Fed. Reg. 11423 (March 8, 2005)

4. In a Medicare Appeal Request dated September 30, 2016, West Cancer Center wrote the following: "alternating electric field therapy (Optune) + adjuvant temozolomide is now an NCCN Category 2A recommendation following post-operative standard brain radiation therapy with concurrent temozolomide." (Exhibit 1, page 24).
5. Letter from the Beneficiary dated December 6, 2016, informed the Medicare Appeals Contractor that TTF was the Beneficiary's best option to treat his condition. He noted the Optune device is covered by many local and national insurance companies and name them within the letter. (Exhibit 1, pages 18-19).
6. Medical records described the Beneficiary as a 68 year-old male with a history of prostate cancer with radiation at the VA. He had persistent headaches with nausea and vomiting and went to the hospital on December 14, 2015, with evidence of vasogenic edema. On February 1, 2016, he was taken for resection and final pathology came back as high grade glioblastoma multiform. Two portions of the tumor were resected from the frontal lobe. Tumor was described as 3.2 x 2.5 x 3 cm via MRI. Beneficiary completed concurrent chemo-radiation with temozolomide on April 12, 2016, and he began maintenance temozolomide on May 12, 2016. The physician prescribed Optune. He indicated he began utilizing TTFields on May 19, 2016, and most recent MRI on August 17, 2016, showed no recurrent or residual disease. (Exhibit 1, pages 24-26).
7. Optune Prescription Form dated March 31, 2017, indicated the physician ordered 6-month prescription for the Beneficiary due to malignant neoplasm of the frontal lobe. (Exhibit 2, page 8).
8. Optune Prescription Form dated September 28, 2017, indicated the physician ordered 6-month prescription for the Beneficiary due to malignant neoplasm of the frontal lobe. (Exhibit 2, page 7).
9. Medical records were provided for May 23, 2017 and June 15, 2017. Treatment history indicated the following: gross resection completed on February 1, 2016. Concurrent chemo radiation with Temodar, completed on April 12th. Optune TTFs completed on May 19, 2016. Temodar treatments were also listed. (Exhibit 2, pages 1-6).
10. Novocure issued invoices for the NOVO-TTF 100A in the amount of \$21,000 for each month of September, October, November, and December. (Exhibit 1, page 32-39).
11. Newly submitted medical records (physician notes) from July 25, 2017, October 17, 2017, December 12, 2017, February 13, 2018, and October 16, 2018, provided treatment record. Treatment plans and medication were listed. (Exhibit 5).
12. Newly submitted medical records (MRI) dated October 13, 2018, showed the Beneficiary had no appreciable evidence of worsening residual or recurrent lesion. (Exhibit 5)
13. National Comprehensive Cancer Network (NCCN) guidelines version 1.2015 provided treatment options for glioblastoma to include chemotherapy or re-irradiation (category 2B) or alternating electric field therapy. (Exhibit 1, pages 54-57).

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

Individuals or organizations dissatisfied with the reconsideration of an initial determination are entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS) provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Act § 1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

On Friday, September 29, 2017, the Centers for Medicare & Medicaid Services (CMS) published the calendar year 2018 amount in controversy (AIC) thresholds for Administrative Law Judge hearings and judicial review. 82 Fed. Reg. 45592 (Sep. 29, 2017). For requests filed on or after January 1, 2018, the AIC threshold for requests for Administrative Law Judge hearings will remain at \$160, and the AIC threshold for seeking judicial review will increase to \$1,600. The notice is available at <https://www.gpo.gov/fdsys/pkg/FR-2017-09-29/pdf/2017-20883.pdf>.

B. Scope of Review

For all appeals stemming from a QIC, the ALJ appeals process is governed by 42 C.F.R. §§ 405.1000 *et seq.* 42 C.F.R. § 405.1032 states, “[t]he issues before the administrative law judge include all the issues brought out in the initial, reconsidered, or revised determination that were not decided entirely in your favor. However, if evidence presented before or during the hearing causes the administrative law judge to question a fully favorable determination, he or she will notify you and will consider it an issue at the hearing.”

C. Standard of Review

The ALJ conducts a de novo review of each claim at issue and issues a decision based on the hearing record. 42 C.F.R. § 405.1000(d) and Section 557 of the Administrative Procedure Act. A de novo review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. All laws and regulations pertaining to the Medicare and Medicaid programs, including, but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations, are binding on ALJ’s. 42 CFR § 405.1063. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. § 405.1018, 42 C.F.R. § 405.1028, and 42 C.F.R. § 405.1030.

II. Principles of Law

A. Statutes and Regulations

Section 1831 of the Act establishes a supplementary insurance program for the aged and disabled. This insurance program, commonly referred to as Part B of Medicare, is financed through premium payments by enrollees together with contributions from funds appropriated by the Federal Government. §1831; 42 U.S.C. 1395j. The program allows for the reimbursement of physicians' services including surgery, consultation, and office visits. §1861(q); 42 U.S.C. 1395x(q)

The standard for payment of these services is found in section 1862(a)(1)(A) of the Act. There, the Act states that no payment may be made "...for items and services...[which] are reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

Section 1833(e) of the Act provides that payment will not be made unless sufficient information is furnished to determine the amounts due to the provider. *See also* 42 CFR §424.5(6).

Section 1862(a)(1)(A) of the Act provides that "[n]otwithstanding any other provision of the Act, no payment shall be made for any expenses incurred for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." *See also* 42 C.F.R. §411.15(k).

Section 1862(a)(12) of the Act provides that no payment may be made for services in connection with the care, treatment, filling, removal, or replacement of teeth or structures directly supporting teeth, except that payment may be made under part A in the case of inpatient hospital services in connection with the provision of such dental services if the individual, because of his underlying medical condition and clinical status or because of the severity of the dental procedure, requires hospitalization in connection with the provision of such services.

Section 1866(a)(1)(A)(i) of the Act provides that "[a]ny provider of services (except a fund designated for purposes of section 1814(g) and section 1835(e)) shall be qualified to participate under this title and shall be eligible for payments under this title if it files with the Secretary an agreement not to charge, except as provided in paragraph (2), any individual or any other person for items or services for which such individual is entitled to have payment made under this title (or for which he would be so entitled if such provider of services had complied with the procedural and other requirements under or pursuant to this title or for which such provider is paid pursuant to the provisions of section 1814(e)) of the Act." *See also* 42 C.F.R. §489.1 *et seq.* (setting forth the terms and limitations on provider agreements).

Section 1879 of the Act limits the liability of the Beneficiary and providers of services if the services are found to be not medically reasonable and necessary under Section 1862(a)(1)(A) or care was custodial in nature under Section 1862(a)(9) of the Act. Payment will only be made pursuant to this section if neither the Beneficiary nor the provider knew or could reasonably have been expected to know that the services were not covered. *See also* 42 C.F.R. §411.404; 42 C.F.R. §411.406.

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (LMRPs) or local coverage determinations (LCDs).

Section 1869(f)(1) of the Act provides that NCDs are binding upon Administrative Law Judges. *See also* 42 CFR §405.1060. *Medicare National Coverage Determinations Manual, Pub. 100-03, Ch. 1, sec. 280* (“NCD 280.1”) provides a mandatory statement as to what constitutes equipment that meets the definition of DME, as follows:

“The term DME is defined as equipment which:

- * Can withstand repeated use; i.e., could normally be rented and used by successive patients;
- * **Is primarily and customarily used to serve a medical purpose;**
- * Generally is not useful to a person in the absence of illness or injury; and,
- * Is appropriate for use in a patient's home.”

Section §1869(f)(2) of the Act provides that Administrative Law Judges will give substantial deference to LCDs, LMRPs, or CMS program guidance when applicable, and if they do not follow the policy they must explain why in their decision. *See also* 42 CFR §405.1062. The Local Coverage Determination Policy applicable to this case. The LCD at issue is L34823 and Policy Article 52711.

L34823

Coverage Indications, Limitations, and/or Medical Necessity

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements.

The purpose of a Local Coverage Determination (LCD) is to provide information regarding “reasonable and necessary” criteria based on Social Security Act § 1862(a)(1)(A) provisions.

In addition to the “reasonable and necessary” criteria contained in this LCD there are other payment rules, which are discussed in the following documents, that must also be met prior to Medicare reimbursement:

- The LCD-related Standard Documentation Requirements Article, located at the bottom of this policy under the Related Local Coverage Documents section.
- The LCD-related Policy Article, located at the bottom of this policy under the Related Local Coverage Documents section.

- Refer to the Supplier Manual for additional information on documentation requirements.
- Refer to the DME MAC web sites for additional bulletin articles and other publications related to this LCD.

For the items addressed in this LCD, the “reasonable and necessary” criteria, based on Social Security Act § 1862(a)(1)(A) provisions, are defined by the following coverage indications, limitations and/or medical necessity.

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

GENERAL

A Detailed Written Order (DWO) (if applicable) must be received by the supplier before a claim is submitted. If the supplier bills for an item addressed in this policy without first receiving a completed DWO, the claim shall be denied as not reasonable and necessary.

An item/service is correctly coded when it meets all the coding guidelines listed in CMS HCPCS guidelines, LCDs, LCD-related Policy Articles, or DME MAC articles. Claims that do not meet coding guidelines shall be denied as not reasonable and necessary/incorrectly coded.

Proof of delivery (POD) is a Supplier Standard and DMEPOS suppliers are required to maintain POD documentation in their files. Proof of delivery documentation must be made available to the Medicare contractor

Policy Article 52711

Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers.

This code is inclusive of all associated supplies necessary for the effective use of code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

Medicare Benefit Policy Manual, Pub. 100-02 (“CMS Pub. 100-02”), Ch. 15, §110.1, also provides guidance pertaining to Medicare coverage of DME, and explains that

Expenses incurred by a beneficiary for the rental or purchases of durable medical equipment (DME) are reimbursable if the following three requirements are met:

- The equipment meets the definition of DME (§110.1);
- The equipment is necessary and reasonable for the treatment of the patient’s illness or injury or to improve the functioning of his or her malformed body member (§110.1); and
- The equipment is used in the patient’s home.

Ch. 15, §110.1(A) further explains as follows:

- **Equipment which is primarily and customarily used for a nonmedical purpose may not be considered "medical" equipment for which payment can be made under the medical insurance program. This is true even though the item has some remote medically related use.** For example, in the case of a cardiac patient, an air conditioner might possibly be used to lower room temperature to reduce fluid loss in the patient and to restore an environment conducive to maintenance of the proper fluid balance. Nevertheless, because the primary and customary use of an air conditioner is a nonmedical one, the air conditioner cannot be deemed to be medical equipment for which payment can be made.
- Other devices and equipment used for environmental control or to enhance the environmental setting in which the beneficiary is placed are not considered covered DME. These include, for example, room heaters, humidifiers, dehumidifiers, and electric air cleaners. Equipment which basically serves comfort or convenience functions or is primarily for the convenience of a person caring for the patient, such as elevators, stairway elevators, and posture chairs, do not constitute medical equipment. Similarly, physical fitness equipment (such as an exercycle), first-aid or precautionary-type equipment (such as preset portable oxygen units), self-help devices (such as safety grab bars), and training equipment (such as Braille training texts) **are considered nonmedical in nature.**

Medicare Program Integrity Manual, Pub. 100-08, ("CMS Pub. 100-08"), Ch. 5, provides guidance as to documentation for DME claims, including the requirement of both physician orders for DME and supporting documentation for medical necessity and delivery. *Ch. 5*, also provides guidance as to patient documentation requirements to support that Medicare coverage criteria for items of DME have been met.

For any DMEPOS [Durable Medical Equipment Prosthetics Orthotics and Supplies] item to be covered by Medicare, the patient's medical record must contain sufficient documentation of the patient's medical condition to substantiate the necessity for the type and quantity of items ordered and for the frequency of use or replacement (if applicable). The information should include the patient's diagnosis and other pertinent information including, but not limited to, duration of the patient's condition, clinical course (worsening or improvement), prognosis, nature and extent of functional limitations, other therapeutic interventions and results, past experience with related items, etc. . . . neither a physician's order nor a CMN [certificate of medical necessity] . . . nor a supplier prepared statement nor a physician attestation by itself provides sufficient documentation of medical necessity, even though it is signed by the treating physician or supplier. There must be information in the patient's medical record that supports the medical necessity for the item and substantiates the answers on the CMN (if applicable) . . . or information on a supplier prepared statement or physician attestation (if applicable). . . . The patient's medical record is not limited to the physician's office records. It may include hospital, nursing home, or HHA records and records from other health care professionals. *CMS Pub. 100-08, Ch. 5, §5.7.*

Medicare Program Integrity Manual, Pub. 100-08 ("CMS Pub. 100-08"), Ch. 13, §13.5.1 explains the reasonable and necessary provisions in LCDs as follows:

Contractors shall describe in the draft LCD the circumstances under which the item or service is reasonable and necessary under 1862(a)(1)(A). Contractors shall consider a service to be reasonable and necessary if the contractor determines that the service is:

- Safe and effective;
- Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary); and
- Appropriate, including the duration and frequency that is considered appropriate for the item or service, in terms of whether it is:
 - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;
 - Furnished in a setting appropriate to the patient's medical needs and condition;
 - Ordered and furnished by qualified personnel;
 - One that meets, but does not exceed, the patient's medical need; and
 - At least as beneficial as an existing and available medically appropriate alternative.

Analysis

The MAC denied coverage because LCD L34823 states TTFT (E0766) will be denied as not reasonable and necessary. The QIC affirmed the denial because there is insufficient documentation to quantify the effects of the device. Appellant argues exact quantification of effectiveness of a treatment is not a requirement for Medicare coverage. The undersigned ALJ agrees with Appellant's argument.

Hearing summary is provided below:

Ms. Miles testified:

Beneficiary was hospitalized in December 2015 after suffering from intense headaches, nausea, and vomiting. He underwent a MRI in January 2016 and he was found to have a mass in a frontal lobe. On February 1, 2016, he underwent a surgical resection and was newly diagnosed with glioblastoma. On April 12, 2016, the Beneficiary underwent chemotherapy and radiation. Beneficiary began using Optune on May 19, 2016. Ms. Miles stated the treatment with Optune was medically reasonable and the best treatment for the Beneficiary.

Beneficiary testified:

The Beneficiary testified he has used the device for approximately three (3) years and the device is working. The last MRI was completed in October 2018 and findings showed the Beneficiary is clear of lesions.

Ms. Parrish argued in support of coverage and stated:

Four (4) CMS medical directors have stated they will be creating a new LCD for newly diagnosed glioblastoma cases but the new LCD will not be completed until 2019.

The TTFT Optune device (E0766) is a portable, wearable medical device that produces alternating electrical fields, tumor treating field (“TTFields”) within the brain by means of electrically insulated surface transducer arrays placed on the scalp. The TTFields disrupt the rapid cell division exhibited by cancer cells supporting tumor growth inhibition without damage to normal neuronal function or structure or any systemic toxicity.

The Appellant submitted documentation confirming the Optune device received an initial April 2011 FDA pre-market approval and later October 2015 FDA pre-market approval supplement. Additional studies and literature have been submitted pertaining to the efficacy of tumor treating fields therapy for indications stated in those FDA approvals, including use of the Optune Device for treatment of recurrent Glioblastoma which has not responded to standard therapy (per the April 2011 FDA approval) and for treatment of newly diagnosed Glioblastoma (per the October 2015 FDA approval supplement). (See CD attachment at Exhibit 5).

Appellant submitted additional and relevant material in support of his appeal such as the article from the Journal of the American Medical Association (JAMA) titled Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide Vs. Temozolomide Alone for Glioblastoma — A Randomized Clinical Trial. The article describes the superior results in progression free survival as well as overall survival of glioblastoma patients using TTFields. This trial shows that the Optune device was safe, non-investigational and effective. And, this trial shows that the Optune device was appropriate for this individual Enrollee's needs, specifically the treatment of newly discovered glioblastoma.

Additional material submitted by the Beneficiary also shows the use of TTFT is generally accepted by the medical community. In the 2016 version of the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology Central Nervous System Cancers guidelines, alternating electric field therapy is a treatment option suggested for glioblastoma: This suggestion was found in a treatment guideline from a national cancer organization, not evidence based on an individual physician treating a single patient in a clinical setting.

Applicable Medicare Regulations: LCD L34823

First, the undersigned notes there is no National Coverage Determination specific to tumor treatment field therapy; therefore, the undersigned looks to the relevant LCD for guidance. Local Coverage Determination L34823, adopted by Medicare Contractors CGS Administrators, LLC and Noridian Healthcare Solutions, LLC (responsible for payment of claims under original Medicare Part B), which became effective January 1, 2017 and as currently in effect, states that “Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.”

An ALJ is not bound by contractor LCDs or CMS program guidance, such as program memoranda and manual instructions, “but will give substantial deference to these policies if they are applicable to a

particular case.” 42 C.F.R. § 405.1062(a). An ALJ must explain the reason for not following such a policy in a specific case. 42 C.F.R. § 405.1062(b). Any decision to disregard a policy “applies only to the specific claim being considered and does not have precedential effect.” (Id.)

Based upon the facts of this case, and after giving appropriate and substantial deference to the LCD policy guidance, I decline to follow the LCD in this case, and instead find that the Optune device was Medically reasonable and necessary as specifically applied to the Beneficiary’s diagnosis and treatment regimen. In declining to follow the pertinent LCD, I have considered the following criteria, as suggested by Medicare manual guidance: (1) whether the device can be expected to make a meaningful contribution to the treatment of the patient’s illness or injury or to the improvement of his or her malformed body member; (2) whether the device can be considered a reasonable treatment, considering expense versus therapeutic benefits, comparative cost of feasible alternatives, and whether the device serves the same purpose as other available equipment or alternatives; (3) whether all features of the device are required for treatment of the Beneficiary’s condition; and, (4) the period of time the DME will be considered medically necessary, which is generally based on the physician’s estimate of the time that his or her patient will need the equipment. *CMS Pub. 100-02, Ch. 15, §110.1(c)*.

Moreover, the LCD, as currently published does not cite any studies, articles or other sources for this determination, or specify any specific diagnoses for which the treatment will be considered as not reasonable and necessary. It makes no distinction between recurrent glioblastoma or newly discovered glioblastoma, and the lack of sources or information on which the determination was based makes it unascertainable. In addition, no reference is made in the LCD Sources of Information and Basis for Decision to several of the more recent studies and guidelines, including the more recent pivotal study and resulting October 2015 FDA pre-market approval supplement allowing the Optune device to be used for newly diagnosed GBM, and the additional even more recent literature and established guidelines supporting such use.

NCCN Guidelines for Anaplastic Gliomas/Glioblastoma for 2017 and 2018 category of evidence 2A (based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate), the Mayo Clinic’s information on Glioblastoma, and the fact that numerous commercial insurers cover the treatment.³ (List of commercial insurers that cover TTFT in CD).

After a careful and thorough review of Appellant’s arguments and the evidence in the record, the undersigned ALJ finds the use of the Optune device for an FDA approved indication was expected to and in fact, did make a significantly meaningful contribution to the treatment of Appellant’s glioblastoma. The physician recommended treatment with the Optune device to halt the progression of his disease which has proven successful. The Beneficiary testified to and the MRI supports that the Beneficiary had no appreciable evidence of worsening residual or recurrent lesion.

The undersigned understand that Medicare often times lags behind other insurers in covering new medical technologies but it is unreasonable to deny Medicare coverage in view of the extensive literature, favorable clinical trials, widespread adoption by other health plans, and NCCN Guidelines support. Therefore, the record supports that the claimed

³ Glioblastoma, Mayo Clinic, *see* <https://www.mayoclinic.org/diseases-conditions/glioblastoma/cdc-20350148>

Optune device treatment was safe and effective, not experimental or investigational, and appropriate. Accordingly, the device is reasonable and necessary for the treatment of Appellant's glioblastoma.

CONCLUSIONS OF LAW

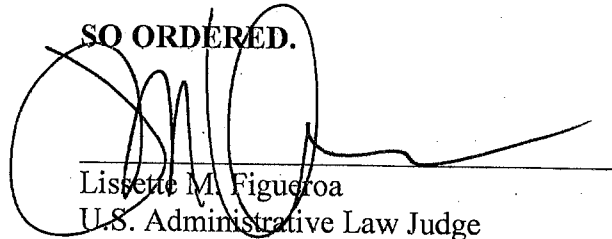
The Appellant's use of the Optune device, HCPCS Code E0766, during dates of service meets requirements for Medicare Part B DME coverage because the device is shown to: meet the definition of durable medical equipment, to have been reasonable and necessary for the treatment of the Beneficiary's GBM, and to have been for use in the Beneficiary's home. *See Sections 1832(a)(1), 1834(a)(13), 1861(n), (s)(6), 1862(a)(1)(A) of Title XVIII 42 C.F.R. §410.38(a); CMS Pub. 100-02, Ch. 15, §110 et seq.*

ORDER

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

Dated: DEC 13 2018

SO ORDERED.



Lissette M. Figueroa
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Cleveland, Ohio

Appeal of: **NOVOCURE INC.**

OMHA Appeal No.: **1-2726630475**

Beneficiary:

Medicare: **Part B**

Medicare No.: *******1268A**

Before: **Paula Gregory**
Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the appellant.

Procedural History

Novocure, Inc. (hereinafter, the appellant), submitted a claim to be reimbursed under Medicare Part B for durable medical equipment (DME) specifically, TTF 100-A and transducer arrays (E1399, A9999) provided to _____ (hereinafter, the beneficiary), on November 19, 2013, November 26, 2013 and December 19, 2013.

The claim was initially denied by the Medicare contractor. On March 18, 2014, the Medicare Administrative Contractor upheld the denial on redetermination. Exh. 1, pp. 14-15. On June 12, 2014, the QIC issued an unfavorable reconsideration and determined that the documentation did not meet the requirements for payment because it did not quantify the effects of the device for the beneficiary or explain why the beneficiary should be considered for this treatment. Exh. 1, pp. 4-7. The appellant was held liable for the cost of the uncovered supplies. *Id.*

The Office of Medicare Hearings and Appeals received the appellant's timely filed appeal on July 11, 2014. Exh. 3, pp. 1-210. Both appeals have been consolidated as requested by the appellant. Exh. 4. The amount in controversy satisfies the jurisdictional requirement for an Administrative Law Judge (ALJ) hearing pursuant to Title XVIII of the Social Security Act (Act) § 1869(b)(1)(E) and 42 C.F.R. § 405.1006.

The appellant submitted documentation to the Administrative Law Judge after the decision from the QIC. The Administrative Law Judge has found that good cause existed for the late submission of this evidence and the evidence has been entered into the record at Exhibit 3.

A hearing was originally scheduled in this matter for September 14, 2018. Notices were issued and no responses were received from CMS or its contractors which indicated an intention to

participate at the hearing. After full review of the record, I find that the evidence supports a fully favorable determination for the Appellant. Therefore, pursuant to Rule 405.1000(g), this decision is issued on the record.

Issue

The issue on appeal is whether payment may be made for the supplies TTF 100-A and transducer arrays (E1399, A9999) provided to the beneficiary on November 19, 2013, November 26, 2013 and December 19, 2013.

Facts

On September 10, 2013 Dr. **Redacted** from the Levine Cancer Institute prescribed the Novo TTF-100A system for treatment of the beneficiary's glioblastoma, ICD-9 code 191.9. Exh. 2, pp. 16-17. On November 11, 2013, the doctor authored a letter that sought predetermination of coverage and payment from the beneficiary's medical provider. Exh. 2, pp. 18-20. In the letter of medical necessity, the doctor indicated that the beneficiary was a good candidate for treatment. *Id.* The letter further indicated that the FDA had approved use of the device for treatment in adult patients with histologically-confirmed glioblastoma multiforme, following histologically or radiologically confirmed recurrence in the supra-tentorial region of the brain after receiving chemotherapy. *Id.* The device was intended to be used as a monotherapy and was intended as an alternative to standard medical therapy for glioblastoma multiforme after surgical and radiation options had been exhausted. *Id.*

The doctor indicated that there were few, if any, available options to the beneficiary. Exh. 2, pp. 18-20. The only other treatment approved by the FDA for recurrent glioblastoma at that time was Avastin. *Id.* The doctor indicated that this medication had never been studied in a randomized trial for recurrent glioblastoma and had not demonstrated a survival time benefit in that population. *Id.* It was her opinion that the Novo TTF-100A system was the only viable treatment option for the beneficiary. *Id.* The beneficiary had exhausted all FDA-approved treatments that could benefit her in her current clinical scenario. *Id.* It was the doctor's belief that the Novo TTF-100A treatment was the only promising treatment option for her. *Id.*

The beneficiary received education and training on the use of her system on September 19, 2013. Exh. 2, pp. 21-24.

The medical record from the Levine Cancer Institute from December 13, 2013 confirmed the beneficiary's treatment history as follows: Exh. 2, p. 33-43.

November 2, 2012, the beneficiary presented to the emergency department with aphasia and nausea. Her symptoms had started on Halloween. She was noted to have a left temporal mass. She was started on AED and steroids.

On November 21, 2012 the beneficiary underwent a craniotomy with subtotal (near-GTR) resection of the left temporal lobe mass.

On December 10, 2012, the beneficiary was started on chemo RT with daily Temodar. The beneficiary was cycled with Temodar doses increased in February, March, April, and

May of 2013. In June, 2013 the beneficiary's 5th cycle of Temodar was held because of a low platelet count.

June 28, 2013, the beneficiary received a blood transfusion. In July 2013 she received her 5th cycle of Temodar. She received her 6th cycle of Temodar in August 2013 when treatment was held due to thrombocytopenia.

September 19, 2013 the beneficiary received a Novo TTF placement. In October, November and December 2013 she was also treated with Avastin.

During the December 16, 2013 visit, it was noted that the beneficiary's NovoTTF was in place. Exh. 2, p. 33-43. The beneficiary was reporting an improvement in her neurological symptoms. *Id.* She was exhibiting less speech slurring and problems with word finding. *Id.* She did not have headaches or seizures although she still had an occasional left eye twitch. *Id.* She had not experienced nosebleeds, coughing up blood, gum bleeding or blood in her urine or stool. *Id.* She was fairly active and was able to walk a mile and a half in the park the day before. *Id.* The plan was to continue the beneficiary's current therapies which included Avastin and NovoTTF. *Id.* A hold was placed on Cytotoxin until the beneficiary's platelet counts were consistently above 50,000. *Id.* A note was made that the beneficiary did not want to restart Cytotoxin any time soon. *Id.* This note was reviewed and signed by Dr. Ashley Sumrall who indicated that she had seen and examined the beneficiary with the physician assistant and agreed with his history, examination, findings and plan. Exh. 2, p. 42.

Legal Framework

I. Administrative Law Judge Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act (Act) § 1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

A hearing before an ALJ is only available if the remaining amount in controversy is \$130 or more. *See* 42 C.F.R. § 405.720, 42 C.F.R. § 405.1002, and 42 C.F.R. § 405.1006. The request for hearing is timely if filed within sixty days after receipt of a QIC decision. *See* 42 C.F.R. § 405.722 and 42 C.F.R. § 405.1002.

B. Scope of Review

"The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in a party's favor . . . However, if evidence presented

before the hearing causes the ALJ to question a favorable portion of the determination, he or she notifies the parties before the hearing and will consider it an issue at the hearing.” 42 C.F.R. § 405.1032.

“If the evidence in the hearing record supports a finding in favor of appellant(s) on every issue, the ALJ may issue a hearing decision without giving the parties prior notice and without holding a hearing.” 42 C.F.R. § 405.1038.

A Medicare Part A Administrative Law Judge Hearing is governed by the procedures set forth at 42 C.F.R. §§ 405.1000 through 405.1054.

C. Standard of Review

The Office of Medicare Hearings and Appeals Administrative Law Judges “conduct impartial ‘de novo’ hearings.” 70 Fed. Reg. 36386 (June 23, 2005).

II. Principles of Law

A. Statutes

Title XVIII § 1832 of the Social Security Act describes the scope of the benefits provided to beneficiaries under Medicare Part B, which includes medical and other health services. Title XVIII § 1861 provides that “medical and other health services” includes durable medical equipment and supplies.

Title XVIII § 1833(e) of the Social Security Act provides that no payment shall be made to any provider of services or other person under this part unless there has been furnished such information as may be necessary in order to determine the amounts due such provider or other person under this part for the period with respect to which the amounts are being paid or for any prior period.

Title XVIII § 1862(a)(1)(A) of the Social Security Act provides that, “Notwithstanding any other provision of this title, no payment may be made under part A or part B for any expenses incurred for items or services . . . which, except for items and services described in a succeeding subparagraph, are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.”

Section 1879 of the Act provides that when Medicare coverage and payment is excluded pursuant to Section 1862(a)(1) or (a)(9), payment may nevertheless be made for items or services, if neither the beneficiary nor the provider or supplier knew, and could not reasonably be expected to have known, that the items or services would not be covered or payable by Medicare.

B. Policy and Guidance

CMS, *Medicare Program Integrity Manual (MPIM) (Internet-Only Manual Publ’n 100-08)* Ch. 5, § 5.7, provides in pertinent part:

For any DMEPOS item to be covered by Medicare, the patient's medical record must contain sufficient documentation of the patient's medical condition to substantiate the necessity for the type and quantity of items ordered and for the frequency of use or replacement (if applicable). The information should include the patient's diagnosis and other pertinent information including, but not limited to, duration of the patient's condition, clinical course (worsening or improvement), prognosis, nature and extent of functional limitations, other therapeutic interventions and results, past experience with related items, etc.

Analysis

On appeal, the QIC denied payment for Novocure TTF 100-A device and transducer array supplies at issue on the basis that the coverage requirements were not met. Exh. 1, pp. 4-7. Specifically the QIC stated that there was insufficient documentation to quantify the effect of the device for this beneficiary, and that the medical records did not support why the beneficiary needed this treatment. *Id.* At the redetermination, the payment was denied because the supplier used a miscellaneous billing code and did not furnish documentation with the manufacturer name, and suggested retail price. Exh. 1, p. 15. The appellant contends the documentation submitted meets coverage criteria for the Novo TTF 100-A system and transducer arrays supplies (E1399, A9999). Exh. 3, pp. 25-26. After careful review of the record, the ALJ disagrees with the QIC and finds that there is sufficient documentation to meet the requirements for Medicare payment of the Novo TTF 100-A system and transducer arrays supplies (E1399, A9999).

The ALJ, after thorough review of the administrative record, finds the appellant has satisfied the Medicare Part B coverage criteria for reimbursement. The treating physician's notes reflected that the beneficiary had recurrent glioblastoma multiforme. Exh. 2, pp. 47-89. Following her diagnosis on November 2, 2012, the beneficiary initially underwent resection and radiation and was also treated with concurrent Temodar chemotherapy. *Id.* The record shows that the chemotherapy was held on June 27, 2013 due to low blood counts. *Id.* The beneficiary received a blood transfusion after which 2 additional cycles of chemotherapy were delivered. *Id.* The chemotherapy was held again on August 8, 2013 due to thrombocytopenia. *Id.* At this point in her therapy, her physician recommended treatment with Novo TTF 100-A system. *Id.* The device was intended to be used as a monotherapy and was intended as an alternative to standard medical therapy for glioblastoma multiforme after surgical and radiation options had been exhausted. Exh. 2, pp. 18-20.

Physician notes indicate that following the Novo TTF device placement on September 19, 2013, the beneficiary showed mild improvements in memory loss, fatigue, appetite and a decrease in seizures. Exh. 2, pp. 53-89. A MRI of the beneficiary's brain conducted on November 30, 2013, indicated a decrease in the tumor size and no new additional lesions, indicating that the Novo TTF device had helped to slow the growth of the tumor. Exh. 2, pp. 80-81. Lastly, a MRI of the beneficiary's brain conducted on January 21, 2014, showed that the recurrent tumor measured 3.8 cm x 1.8 cm which is only slightly larger than the measured tumor size on November 30, 2013, again indicating that the Novo TTF device had helped to slow the growth of the tumor. Exh. 2, pp. 61-62.

Here, coverage criteria have been met and the detailed medical records contain a letter of medical necessity from the physician with the rationale for the device in addition to the prescription and order form. Exh. 2, pp. 16-20.

Because the claim is covered by Medicare, the issue of liability is not addressed.

Conclusions of Law

Payment may be made for the Novo TTF 100-A system and transducer arrays supplies (E1399, A9999).

Order


The Medicare Contractor is directed to process the claim in accordance with this decision.

SO ORDERED

Dated:

11/30/2018

Paula Gregory
Paula Gregory
Administrative Law Judge

 <p align="center">U.S. Department of Health and Human Services OFFICE OF MEDICARE HEARINGS AND APPEALS Southern Region Miami, FL</p>	
Appeal of:	ALJ Appeal No: 1-7901585879
Beneficiary:	MEDICARE Part B
HICN:	Before: Kurt Gronau U.S. Administrative Law Judge

I. SUMMARY OF DECISION

After conducting a de novo, on the record, review of the evidence, a **FULLY FAVORABLE** decision is entered in the appeal of Medicare Beneficiary (Appellant).

II. STATEMENT OF THE CASE **(PROCEDURAL HISTORY)**

A claim was filed on behalf of Medicare Beneficiary with CGS Administrators, for Tumor Treatment Filed Therapy (E0766) provided from December 8, 2017 to February 8, 2018. CGS denied the claim initially and on redetermination. On September 5, 2018, C2C Solutions, Inc., the Medicare Qualified Independent Contractor (QIC) denied the claim holding that the medical documentation does not support the need for the device, which is required as outlines in the IOM and NCD and there is insufficient documentation to quantify the effects of the device for the Beneficiary (Ex. 1, p. 4).

The Appellant filed a request for Medicare hearing before an administrative law judge (ALJ), which was timely¹ received by the Office of Medicare Hearings and Appeals (OMHA). The request for the ALJ hearing meets the amount in controversy requirement. Therefore, the jurisdictional predicates for a hearing before OMHA have been satisfied² and the request for an appeal of the unfavorable decision regarding whether Medicare coverage guidelines have been met for payment of the Tumor Treatment Field Therapy device (E0766), which is covered by this decision, is properly before the ALJ for de novo review. The Appellant submitted addition clinical studies, NCCN Guidelines, payer policies, FDA approvals and statement of adoption, which are entered as Exhibit 4.

Upon reviewing the documentation submitted, the undersigned ALJ has decided to issue an on-the-record fully favorable decision. Pursuant to 42 CFR §405.1038, when the documentary

¹ 42 C.F.R. § 405.1002(a)(1).

² 42 C.F.R. § 478.44.

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evidence supports a finding fully favorable to the appellant(s), an ALJ may issue an on-the-record decision.

III. ISSUES

The issue to be determined by the ALJ is whether payment can be made under Part B of Title XVIII of the Act for the B for Tumor Treatment Field Therapy (E0766) provided to the Beneficiary from December 8, 2017 to February 8, 2018, and if not, to determine who is responsible for the bill.

IV. FINDINGS OF FACT

The Beneficiary suffers from glioblastoma, an aggressive form of brain cancer (Ex. 2, pp. 1-55; Ex. 3, pp. 1-8). After surgery and concurrent chemotherapy and radiation, his clinician prescribed tumor treatment field therapy (TTFT) from December 8, 2017 to February 8, 2018 (Ex. 3, pp. 1-3).

V. LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act §1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated her authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. See, 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. (*Id.*).

To be entitled to a hearing before an ALJ, a party must meet the minimum amount in controversy requirement. 42 C.F.R. § 405.1006. The amount in controversy threshold for ALJ hearing requests filed on or after January 1, 2010, is \$130. 74 Fed. Reg. 48976 (September 25, 2009). The request for hearing is timely if filed within sixty days after receipt of a QIC Reconsideration. See, 42 CFR § 405.1002(a)(1).

B. Scope of Review

For all appeals stemming from a QIC, the ALJ appeals process is governed by 42 CFR §§405.1000 *et seq.* 42 CFR § 405.1032 states, "[t]he issues before the administrative law judge include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in your favor. However, if evidence presented before or during the hearing causes the administrative law judge to question a fully favorable determination, he or she will notify you and will consider it an issue at the hearing."

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C. Standard of Review

"The [Office of Medicare Hearings and Appeals]...is staff[ed] with Administrative Law Judges who conduct 'de novo' hearings...." 70 Fed. Reg. 36386 (June 23, 2005); See also, In re Atlantic Anesthesia Associates, P.C., MAC (June 2004) ("An ALJ qualified and appointed pursuant to the Administrative Procedure Act acts as an independent finder of fact in conducting a hearing pursuant to § 1869 of the Act. This requires *de novo* consideration of the facts and law.")

II. Principles of Law

A. Statutes and Regulations

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services (CMS).

Title XVIII of the Social Security Act (the Act) §1831 established the Supplemental Medical Insurance Program for the aged and disabled under Part B.

Section 1832 of the Act and 42 C.F.R. §410.3 establish the scope of benefits that are provided to beneficiaries under the Medicare Part B insurance program. Under §1832(a)(2)(B) of the Act, an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with them made by a provider of services.

Section 1833(e) of the Act and 42 C.F.R. §424.5(6) provide that payment will not be made unless sufficient information exists to determine whether payment is due the amount that should be paid.

Section 1862(a)(1) of the Act states the items and services that are reasonable and necessary for the diagnosis and treatment of illness or injury are covered under the Medicare Program.

Section 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Act and Medicare Regulations at 42 C.F.R. §410.10(h) provide that covered "medical and other health services" under Medicare Part B include, among many other things, durable medical equipment.

Sections 1832(a)(2)(G), 1861(n), and 1862(a)(1)(A) of the Act provide that Part B covers diabetic testing supplies that are reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. A claim for such supplies must include the physician's order, date on or before the delivery of the item, and sufficient medical evidence to justify it. See Section 1833(3) of the Act.

Section 1833(e) of the Act provides that "[n]o payment shall be made to any provider of services... unless there has been furnished such information as may be necessary in order to determine the amounts due such provider . . .". See also 42 C.F.R. §424.5(a)(6); CMS Medicare Program Integrity Manual, Publication 100-08, Chapter 5, §5.7 (When specific data is requested, it must be provided. If the data is not provided the claim will [be denied] for medical necessity.).

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Section 1862(a)(1)(A) of Title XVIII and Medicare Regulations at 42 C.F.R. §411.15(k)(1) further provides that otherwise covered services which are determined to be not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, will also be excluded from coverage under the Medicare Program.

Section 1879 of Title XVIII limits the liability of the beneficiary and suppliers of items if the items are found to be not medically reasonable and necessary under §1862(a)(1)(A). Payment will only be made pursuant to this section if neither the beneficiary nor the provider knew or could reasonably have been expected to know that the items were not covered. See also 42 C.F.R. §411.404 and 42 C.F.R. §411.406.

1. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. Section 1869(f)(1) of the Act provides that National Coverage Determinations are binding upon ALJs. See also, 42 CFR §405.1060.

In addition to binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals, local medical review policies (LMRPs) and local coverage determinations (LCDs). Section 1869(f)(2) of the Act provides that ALJs will give substantial deference to local coverage determinations (LCDs), local medical review policies (LMRPs), or CMS program guidance when applicable, and if they do not follow the policy they must explain why in their decision. See also, 42 CFR §405.1062; Shalala v. Guernsey Mem. Hosp., 514 U.S. 87, 97, 99 (1995) (an agency may issue interpretive rules to advise the public of its construction of the statutes and rules that it administers).

Specific to the instant case is the CMS Medicare National Coverage Determination Manual, Pub. 100-3, Chapter 1, §280.1 and it states, in part, as follows:

When the A/B MAC (HHH) or DME MAC receives a claim for an item of equipment which does not appear to fall logically into any of the generic categories listed, the A/B MAC (HHH) or DME MAC has the authority and responsibility for deciding whether those items are covered under the DME benefit. These decisions must be made by each A/B MAC (HHH) and DME MAC based on the advice of its medical consultants, taking into account:

- The Medicare Claims Processing Manual, Chapter 20, "Durable Medical Equipment, Prosthetics and Orthotics, and Supplies (DMEPOS)."
- Whether the item has been approved for marketing by the Food and Drug Administration (FDA) and is otherwise generally considered to be safe and effective for the purpose intended; and
- Whether the item is reasonable and necessary for the individual patient. The term DME is defined as equipment which:

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- Can withstand repeated use; i.e., could normally be rented and used by successive patients;
- Is primarily and customarily used to serve a medical purpose;
- Generally is not useful to a person in the absence of illness or injury; and,
- Is appropriate for use in a patient's home.

Also relevant is LCD L34823, Tumor Treatment Field Therapy (TTFT).

VI. ANALYSIS

After conducting a de novo, on the record, review of the evidence, the undersigned ALJ finds that Medicare coverage requirements have been met for payment of Tumor Treatment Field Therapy device (E0766) provided to the Beneficiary from December 8, 2017 to February 8, 2018. The QIC denied the claim holding that the medical documentation does not support the need for the device, which is required as outlines in the IOM and NCD and there is insufficient documentation to quantify the effects of the device for the Beneficiary (Ex. 1, p. 4).

LCD L34823 states that tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers. This code is inclusive of all associated supplies necessary for the effective use of code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

The Beneficiary suffers from glioblastoma, an aggressive form of brain cancer (Ex. 2, pp. 1-55; Ex. 3, pp. 1-8). After surgery and concurrent chemotherapy and radiation, his clinician prescribed tumor treatment field therapy (TTFT) therapy from December 8, 2017 to February 8, 2018 (Ex. 3, pp. 1-3). TTFT disrupts and corrupts the division of cancer cells and leads to the death of such cells (Id.). The FDA has approved the treatment, under the brand name, Optune, for adult patients (22 years of age or older) with histologically-confirmed glioblastoma (GBM), and TTFT with temozolomide (TMZ) for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard care chemotherapy (Id.).

At this time, an Order and Optune Prescription form was completed for an Optune TTFT device on March 30, 2017 and December 1, 2017 (Ex. 2, pp. 5-6). It was signed by Dr. MD (Id.). An Assessment of Need was also completed on June 2, 2017 (Ex. 2, p. 7). The TTFT device was provided to the Beneficiary from December 8, 2017 to February 8, 2018 (Ex. 2, p. 18).

In 2011 and 2013, the FDA approved, through its most rigorous review process, a device to deliver TTFT, finding it to be safe and effective for the treatment of glioblastoma (Ex. 3, p. 1). Published, peer review literature shows improved clinical outcome of patients who receive TTFT for their glioblastoma (Ex. 4). TTFT for glioblastoma is included in the National Comprehensive Cancer

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Network guidelines (Id.). The FDA has also approved the device for newly diagnosed glioblastoma and recurrent glioblastoma (Id.).

Based on the foregoing, the undersigned ALJ finds the Appellant has complied with all Medicare rules and regulations. The Beneficiary suffered from glioblastoma, an aggressive form of brain cancer. The Beneficiary had previous therapy, which was unsuccessful. As such, an order was completed for a TTFT device, which was provided from December 8, 2017 to February 8, 2018. The device is considered safe and effective and approved by the FDA for glioblastomas. As Medicare rules and guidelines have been met, payment is due and owing for this claim.

VII. CONCLUSION

Medicare statutory requirements and guidelines have been met for the Tumor Treatment Field Therapy device (E0766) provided to the Beneficiary from December 8, 2017 to February 8, 2018. As such, payment is due and owing.


VIII. ORDER

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: _____

OCT 10 2018


Kurt Gronau
U.S. Administrative Law Judge



**U.S. Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Southern Region
Miami, FL**

Appeal of:

ALJ Appeal No: **1-7789988527**

Beneficiary:

MEDICARE Part B

HICN:

Before: **Kurt Gronau**
U.S. Administrative Law Judge

I. SUMMARY OF DECISION

After conducting a de novo review of the evidence, a **FULLY FAVORABLE** decision is entered in the appeal of Medicare Beneficiary (Appellant).

II. STATEMENT OF THE CASE **(PROCEDURAL HISTORY)**

A claim was filed on behalf of Medicare Beneficiary 1 with CGS Administrators, for Tumor Treatment Filed Therapy (E0766) provided on August 7, 2017. CGS denied the claim initially and on redetermination. On June 15, 2018, C2C Solutions, Inc., the Medicare Qualified Independent Contractor (QIC) denied the claim holding that the medical documentation does not support the need for the device, which is required as outlines in the IOM and NCD and there is insufficient documentation to quantify the effects of the device for the Beneficiary (Ex. 1, p. 4).

The Appellant filed a request for Medicare hearing before an administrative law judge (ALJ), which was timely¹ received by the Office of Medicare Hearings and Appeals (OMHA). The request for the ALJ hearing meets the amount in controversy requirement. Therefore, the jurisdictional predicates for a hearing before OMHA have been satisfied² and the request for an appeal of the unfavorable decision regarding whether Medicare coverage guidelines have been met for payment of the Tumor Treatment Field Therapy device (E0766), which is covered by this decision, is properly before the ALJ for de novo review. The Appellant submitted additional clinical studies, NCCN Guidelines, payer policies, FDA approvals and statement of adoption, which are entered as Exhibit 4.

A hearing was held on September 19, 2018 with telephonic participation by Debra Parrish, Esq. and Judtin Kelly, RN on behalf of the Appellant. The participants were sworn in and Exhibits 1 (procedural records), 2 (medical records), and 3 (Notice of Hearing and Response to Notice of

¹ 42 C.F.R. § 405.1002(a)(1).

² 42 C.F.R. § 478.44.

Hearing) were entered into evidence without objection. The Appellants moved to allow additional medical and supporting medical documents into the record and the undersigned ALJ agreed to allow the Appellant to supplement the record. These documents, marked as Exhibit 4, were entered into evidence.

III. ISSUES

The issue to be determined by the ALJ is whether payment can be made under Part B of Title XVIII of the Act for the B for Tumor Treatment Filed Therapy (E0766) provided to the Beneficiary on August 7, 2017, and if not, to determine who is responsible for the bill.

IV. FINDINGS OF FACT

The Beneficiary suffers from glioblastoma, an aggressive form of brain cancer, diagnosed in March of 2017 (Ex. 2, pp. 1-168; Ex. 3, pp. 1-8). After surgery and concurrent chemotherapy and radiation, his clinician prescribed tumor treatment field therapy (TTFT) on August 7, 2017 (Ex. 3, pp. 1-3).

V. LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act §1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated her authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See*, 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. (*Id.*).

To be entitled to a hearing before an ALJ, a party must meet the minimum amount in controversy requirement. 42 C.F.R. § 405.1006. The amount in controversy threshold for ALJ hearing requests filed on or after January 1, 2010, is \$130. 74 Fed. Reg. 48976 (September 25, 2009). The request for hearing is timely if filed within sixty days after receipt of a QIC Reconsideration. *See*, 42 CFR § 405.1002(a)(1).

B. Scope of Review

For all appeals stemming from a QIC, the ALJ appeals process is governed by 42 CFR §§405.1000 *et seq.* 42 CFR § 405.1032 states, “[t]he issues before the administrative law judge include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in your favor. However, if evidence presented before or during the hearing causes the

administrative law judge to question a fully favorable determination, he or she will notify you and will consider it an issue at the hearing.”

C. Standard of Review

“The [Office of Medicare Hearings and Appeals]...is staff[ed] with Administrative Law Judges who conduct ‘de novo’ hearings....” 70 Fed. Reg. 36386 (June 23, 2005); See also, In re Atlantic Anesthesia Associates, P.C., MAC (June 2004) (“An ALJ qualified and appointed pursuant to the Administrative Procedure Act acts as an independent finder of fact in conducting a hearing pursuant to § 1869 of the Act. This requires *de novo* consideration of the facts and law.”)

II. Principles of Law

A. Statutes and Regulations

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services (CMS).

Title XVIII of the Social Security Act (the Act) §1831 established the Supplemental Medical Insurance Program for the aged and disabled under Part B.

Section 1832 of the Act and 42 C.F.R. §410.3 establish the scope of benefits that are provided to beneficiaries under the Medicare Part B insurance program. Under §1832(a)(2)(B) of the Act, an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with them made by a provider of services.

Section 1833(e) of the Act and 42 C.F.R. §424.5(6) provide that payment will not be made unless sufficient information exists to determine whether payment is due the amount that should be paid.

Section 1862(a)(1) of the Act states the items and services that are reasonable and necessary for the diagnosis and treatment of illness or injury are covered under the Medicare Program.

Section 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Act and Medicare Regulations at 42 C.F.R. §410.10(h) provide that covered “medical and other health services” under Medicare Part B include, among many other things, durable medical equipment.

Sections 1832(a)(2)(G), 1861(n), and 1862(a)(1)(A) of the Act provide that Part B covers diabetic testing supplies that are reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. A claim for such supplies must include the physician’s order, date on or before the delivery of the item, and sufficient medical evidence to justify it. See Section 1833(3) of the Act.

Section 1833(e) of the Act provides that “[n]o payment shall be made to any provider of services. . . unless there has been furnished such information as may be necessary in order to determine the amounts due such provider . . .”. See also 42 C.F.R. §424.5(a)(6); CMS Medicare Program Integrity Manual, Publication 100-08, Chapter 5, §5.7 (When specific data is requested, it must be provided. If the data is not provided the claim will [be denied] for medical necessity.).

Section 1862(a)(1)(A) of Title XVIII and Medicare Regulations at 42 C.F.R. §411.15(k)(1) further provides that otherwise covered services which are determined to be not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, will also be excluded from coverage under the Medicare Program.

Section 1879 of Title XVIII limits the liability of the beneficiary and suppliers of items if the items are found to be not medically reasonable and necessary under §1862(a)(1)(A). Payment will only be made pursuant to this section if neither the beneficiary nor the provider knew or could reasonably have been expected to know that the items were not covered. See also 42 C.F.R. §411.404 and 42 C.F.R. §411.406.

1. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. Section 1869(f)(1) of the Act provides that National Coverage Determinations are binding upon ALJs. See also, 42 CFR §405.1060.

In addition to binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals, local medical review policies (LMRPs) and local coverage determinations (LCDs). Section 1869(f)(2) of the Act provides that ALJs will give substantial deference to local coverage determinations (LCDs), local medical review policies (LMRPs), or CMS program guidance when applicable, and if they do not follow the policy they must explain why in their decision. See also, 42 CFR §405.1062; Shalala v. Guernsey Mem. Hosp., 514 U.S. 87, 97, 99 (1995) (an agency may issue interpretive rules to advise the public of its construction of the statutes and rules that it administers).

Specific to the instant case is the CMS Medicare National Coverage Determination Manual, Pub. 100-3, Chapter 1, §280.1 and it states, in part, as follows:

When the A/B MAC (HHH) or DME MAC receives a claim for an item of equipment which does not appear to fall logically into any of the generic categories listed, the A/B MAC (HHH) or DME MAC has the authority and responsibility for deciding whether those items are covered under the DME benefit. These decisions must be made by each A/B MAC (HHH) and DME MAC based on the advice of its medical consultants, taking into account:

- The Medicare Claims Processing Manual, Chapter 20, "Durable Medical Equipment, Prosthetics and Orthotics, and Supplies (DMEPOS)."
- Whether the item has been approved for marketing by the Food and Drug Administration (FDA) and is otherwise generally considered to be safe and effective for the purpose intended; and
- Whether the item is reasonable and necessary for the individual patient. The term DME is defined as equipment which:

- Can withstand repeated use; i.e., could normally be rented and used by successive patients;
- Is primarily and customarily used to serve a medical purpose;
- Generally is not useful to a person in the absence of illness or injury; and,
- Is appropriate for use in a patient's home.

Also relevant is LCD L34823, Tumor Treatment Field Therapy (TTFT).

VI. ANALYSIS

After conducting a de novo review of the evidence, the undersigned ALJ finds that Medicare coverage requirements have been met for payment of Tumor Treatment Field Therapy device (E0766) provided to the Beneficiary on August 7, 2017. The QIC denied the claim holding that the medical documentation does not support the need for the device, which is required as outlined in the IOM and NCD and there is insufficient documentation to quantify the effects of the device for the Beneficiary (Ex. 1, p. 4). LCD L34823 states that tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers. This code is inclusive of all associated supplies necessary for the effective use of code E0766 including, but not limited to, transducers/surface electrodes, lead wires, adhesive patches, connectors, conductive gel and skin preps.

The Beneficiary suffers from glioblastoma, an aggressive form of brain cancer (Ex. 2, pp. 1-168; Ex. 3, pp. 1-8). After surgery and concurrent chemotherapy and radiation, his clinician prescribed tumor treatment field therapy (TTFT) therapy on August 7, 2017 (Ex. 3, pp. 1-3). TTFT disrupts and corrupts the division of cancer cells and leads to the death of such cells (Id.). The FDA has approved the treatment, under the brand name, Optune, for adult patients (22 years of age or older) with histologically-confirmed glioblastoma (GBM), and TTFT with temozolomide (TMZ) for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard care chemotherapy (Id.).

At this time, an Order and Optune Prescription form was completed for an Optune TTFT device on July 17, 2017 (Ex. 2, pp. 1-2). It was signed by Dr. MD (Id.). An Assessment of Need was also completed on July 31, 2017 (Ex. 2, p. 7). Dr. Lu-Emerson also submitted a Letter of Medical Necessity due to Life Threatening Condition on April 2, 2018 (Ex. 2, pp. 3-5). The TTFT device was provided to the Beneficiary on August 7, 2017 (Ex. 2, p. 18). Mr. Kelly testified about the device and its effectiveness and categorization (Ex. Hearing CD). He explained that guidelines were updated in 2015 from the 2011 FDA guidelines regarding glioblastomas and treatments (Id.). A December 2017 MRI revealed the cancer as stable (Ex. Hearing CD). The Appellant underwent surgical resection with radiation in 2018 (Id.). Another MRI in May of 2018 again showed the glioblastoma as stable (Id.).

In 2011 and 2013, the FDA approved, through its most rigorous review process, a device to deliver TTFT, finding it to be safe and effective for the treatment of glioblastoma (Ex. 3, p. 1). Published, peer review literature shows improved clinical outcome of patients who receive TTFT for their glioblastoma (Ex. 4). TTFT for glioblastoma is included in the National Comprehensive Cancer Network guidelines (Id.). The FDA has also approved the device for newly diagnosed glioblastoma and recurrent glioblastoma (Id.; Hearing CD). The Appellant submitted additional documentation supporting that TTFT with temozolomide (TMZ) is covered for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy (Ex. 4, p. 1). The treatment showed effectiveness per two MRIs in December 2017 and May 2018, showing the glioblastoma as stable without spread (Ex. Hearing CD).

Based on the foregoing, the undersigned ALJ finds the Appellant has complied with all Medicare rules and regulations. The Beneficiary suffered from glioblastoma, an aggressive form of brain cancer, which was diagnosed in March of 2017 (Ex. Hearing CD). The Beneficiary had previous therapy, which was unsuccessful. As such, an order was completed for a TTFT device, which was provided on August 7, 2017. The device is considered safe and effective and approved by the FDA for glioblastomas. As Medicare rules and guidelines have been met, payment is due and owing for this claim.

VII. CONCLUSION

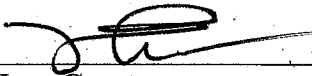
Medicare statutory requirements and guidelines have been met for the Tumor Treatment Field Therapy device (E0766) provided to the Beneficiary on August 7, 2017. As such, payment is due and owing.

VIII. ORDER

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: DEC 20 2018



Kurt Gronau
U.S. Administrative Law Judge



**U.S. Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Southern Region
Miami, FL**

Appeal of:

ALJ Appeal No: **1-7835292741**

Beneficiary:

Medicare Part B

HICN:

Before: **Kurt Gronau**
U.S. Administrative Law Judge

I. SUMMARY OF DECISION

After conducting a de novo review of the evidence, a **FULLY FAVORABLE** decision is entered in the appeal of Medicare Beneficiary (Appellant).

II. STATEMENT OF THE CASE **(PROCEDURAL HISTORY)**

A claim was filed for electrical stim cancer treatment (E0766) provided from September 27, 2017 through December 27, 2017. The claim was denied initially and at redetermination. The QIC denied the claim holding that pursuant to LCD L34823 the medical necessity is not established as the medical records do not quantify the effects of the device for the Appellant or explain why the Appellant should be considered for this treatment (Exh. 1, p. 4).

The Appellant timely¹ filed a request for Medicare hearing before an ALJ with OMHA. The request meets the amount in controversy.² Therefore the jurisdictional requirements for a hearing before OMHA have been satisfied and the request for an appeal of the unfavorable decision regarding whether Medicare coverage guidelines have been met for coverage of the E0766 treatment, which is covered by this decision, is properly before the ALJ for de novo review.

A hearing was held on October 15, 2018 with telephonic participation by Debra Parrish, Esq. on behalf of the Appellant, Dan McCoy and Julie Miles, RN, on behalf of Novocare. The participants were sworn in and Exhibits 1 (procedural documents), 2 (medical records), 3 (Request for ALJ Hearing), and 4 (OMHA proceedings).

¹ 42 C.F.R. § 405.1002(a)(1).

² 42 C.F.R. § 478.44.

III. ISSUES

The issue to be determined by the ALJ is whether coverage can be extended under Part B of Title XVIII of the Act for electrical stim cancer treatment (E0766) provided from September 27, 2017 through December 27, 2017, and if not, to determine who is responsible for the bill.

IV. FINDINGS OF FACT

The Appellant suffered from high-grade glioma (Exh. 2, p. 2). He originally presented with neurologic deficits with speech difficulty and symptoms persisted for some time. *Id.* He underwent workup and was found to have a 4.7 cm left medial temporal mass with extensive vasogenic edema and a small midline shift. *Id.* He underwent resection on November 23, 2016 with pathology demonstrating high-grade glioma. *Id.* His medical history was significant for MI, mitral valve insufficiency that was repaired at the same time he had a single vessel CABG (Exh. 2, pp. 2-3). An order was completed for Optune February 7, 2017 and August 23, 2017 (Exh. 2, pp. 5-6). An Assessment of need was completed on February 10, 2017 (Exh. 2, p. 7). The device was first delivered on February 27, 2017 (Exh. 2, p. 23). At the hearing, it was argued that Optune is FDA approved and that it is efficacious for this Appellant as he continues to use it and continues to live.

V. LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act §1869(b)(1)(A).

In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See*, 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

To be entitled to a hearing before an ALJ, a party must meet the minimum amount in controversy requirement. 42 C.F.R. § 405.1006. The amount in controversy threshold for ALJ hearing requests filed on or after January 1, 2010, is \$130. 74 Fed. Reg. 48976 (September 25, 2009). The request for hearing is timely if filed within sixty days after receipt of a QIC Reconsideration. *See*, 42 CFR § 405.1002(a)(1).

B. Scope of Review

For all appeals stemming from a QIC, the ALJ appeals process is governed by 42 CFR §§405.1000 *et seq.* 42 CFR § 405.1032 states, “[t]he issues before the administrative law judge include all the issues brought out in the initial, reconsidered or revised determination that were not decided

entirely in your favor. However, if evidence presented before or during the hearing causes the administrative law judge to question a fully favorable determination, he or she will notify you and will consider it an issue at the hearing.”

C. Standard of Review

“The [Office of Medicare Hearings and Appeals]...is staff[ed] with Administrative Law Judges who conduct ‘de novo’ hearings....” 70 Fed. Reg. 36386 (June 23, 2005); See also, In re Atlantic Anesthesia Associates, P.C., MAC (June 2004) (“An ALJ qualified and appointed pursuant to the Administrative Procedure Act acts as an independent finder of fact in conducting a hearing pursuant to § 1869 of the Act. This requires *de novo* consideration of the facts and law.”)

II. Principles of Law

A. Statutes and Regulations

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services (CMS).

Title XVIII of the Social Security Act (the Act) §1831 established the Supplemental Medical Insurance Program for the aged and disabled under Part B.

Section 1832 of the Act and 42 C.F.R. §410.3 establish the scope of benefits that are provided to beneficiaries under the Medicare Part B insurance program. Under §1832(a)(2)(B) of the Act, an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with them made by a provider of services.

Section 1833(e) of the Act and 42 C.F.R. §424.5(6) provide that payment will not be made unless sufficient information exists to determine whether payment is due the amount that should be paid.

Section 1862(a)(1) of the Act states the items and services that are reasonable and necessary for the diagnosis and treatment of illness or injury are covered under the Medicare Program.

Section 1879 of the Act and 42 C.F.R. §411.400 provide conditions for payment and limits the liability of the beneficiary and providers of services if the services are found to be not medically reasonable and necessary under §1862(a)(1)(A) or care was custodial in nature under §1862(a)(1)(9). Payment will only be made pursuant to section 1879 if neither the beneficiary nor the provider knew or could reasonably have been expected to know that the services were not covered.

42 C.F.R. §424.5 requires that the provider, supplier, or beneficiary must supply sufficient information to determine whether payment is due and the amount.

42 C.F.R. §405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs), or Center for

Medicare Services (“CMS”) program guidance when applicable. An explanation in the decision is required if the judge does not follow these policies.

1. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. Section 1869(f)(1) of the Act provides that National Coverage Determinations are binding upon ALJs. See also, 42 CFR §405.1060. There is no NCD that applies to the medical services at issue in this case.

In addition to binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals, local medical review policies (LMRPs) and local coverage determinations (LCDs). Section 1869(f)(2) of the Act provides that ALJs will give substantial deference to local coverage determinations (LCDs), local medical review policies (LMRPs), or CMS program guidance when applicable, and if they do not follow the policy they must explain why in their decision. See also, 42 CFR §405.1062; Shalala v. Guernsey Mem. Hosp., 514 U.S. 87, 97, 99 (1995) (an agency may issue interpretive rules to advise the public of its construction of the statutes and rules that it administers).

The CMS Medicare Program Integrity Manual (Internet-Only Publ’n 100-08), Chapter 3, §3.11, explains that “[f]or Medicare to consider coverage and payment for any item or service, the information submitted by the supplier or provider [] must be corroborated by the documentation in the patient’s medical records that Medicare coverage criteria have been met.” It continues that the patient’s medical records must be maintained by the physician, provider, and/or supplier and that they must be available to the contractor upon request. Moreover, sufficient documentation is required in order to confirm that an item or service was actually provided and billed at the appropriate level.

The undersigned ALJ gave substantial deference to LCD L34823.

VI. ANALYSIS

After conducting a de novo, on the record, review of the evidence, the undersigned ALJ finds that Medicare coverage requirements have been met for coverage of electrical stim cancer treatment (E0766) provided from September 27, 2017 through December 27, 2017. The QIC denied the claim holding that pursuant to LCD L34823 the medical necessity is not established as the medical records do not quantify the effects of the device for the Appellant or explain why the Appellant should be considered for this treatment (Exh. 1, p. 4).

In the instant matter, the Appellant suffered from high-grade glioma (Exh. 2, p. 2). He originally presented with neurologic deficits with speech difficulty and symptoms persisted for some time. Id. He underwent workup and was found to have a 4.7 cm left medial temporal mass with extensive vasogenic edema and a small midline shift. Id. He underwent resection on November 23, 2016

with pathology demonstrating high-grade glioma. *Id.* His medical history was significant for MI, mitral valve insufficiency that was repaired at the same time he had a single vessel CABG (Exh. 2, pp. 2-3). An order was completed for Optune February 7, 2017 and August 23, 2017 (Exh. 2, pp. 5-6). An Assessment of need was completed on February 10, 2017 (Exh. 2, p. 7). The device was first delivered on February 27, 2017 (Exh. 2, p. 23). At the hearing, it was argued that Optune is FDA approved and that it is efficacious for this Appellant as he continues to use it and continues to live.

The CMS *MCPM, supra.*, Ch. 3, §3.11, explains that “[f]or Medicare to consider coverage and payment for any item or service, the information submitted by the supplier or provider [] must be corroborated by the documentation in the patient’s medical records that Medicare coverage criteria have been met.” LCD L34823 states that tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. The LCD only provides a conclusory statement and does not elaborate further as to why E0766 treatment is not reasonable and necessary. Section 1862(1)(A) of the Act states that no payment may be made under part A or part B for any expenses incurred for items or services, which “are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.”

Although LCD L34823 states that E0766 treatment is not reasonable and necessary, the facts of this case demonstrate that the treatment is FDA approved and is efficacious for the Appellant as he continues to use it and continues to live. The regulation at 42 CFR § 405.1062 states an ALJ is not bound by an LCD, but must provide the reasons why the policy was not followed. The record demonstrates the Appellant suffered from high-grade glioma, is treated with E0766 therapy since 2017, and that the treatment is successful as he continues to live. Accordingly, this treatment complies with § 1862(1)(A) of the Act and the CMS *MCPM, supra.*, Ch. 3, §3.11. Therefore, medical necessity has been established and the undersigned ALJ finds the Appellant has complied with Medicare rules and guidelines for the electrical stim cancer treatment (E0766) provided from September 27, 2017 through December 27, 2017. As such, coverage is due and owing for this claim.

VII. CONCLUSION

Medicare statutory requirements and guidelines have been met for coverage of electrical stim cancer treatment (E0766) provided from September 27, 2017 through December 27, 2017. As such, coverage must remain denied. As such, coverage must be extended for this claim.

VIII. ORDER

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: _____

OCT 29 2018



Kurt Gronau
U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Arlington, Virginia**

Appellant:	ALJ Appeal No.: 1-7103887851
Beneficiary:	Medicare Part: C
HICN: * 9295B1	Before: Jeffrey S. Gulin U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments provided in the record, a **FAVORABLE** decision is entered for ("Appellant").

PROCEDURAL HISTORY

I ("Enrollee/Beneficiary") was enrolled in the Health Net of California health plan ("Plan"). The Appellant is requesting the Plan to pre-approve an Optune device. The Plan denied the request. The Appellant requested reconsideration from Maximus Federal Services, the Part C Qualified Independent Contractor ("QIC"). The QIC indicated that the Plan contract covers services in accordance with Medicare rules, and found that the Plan does not have to pre-approve an Optune device.

On December 20, 2017, the Office of Medicare Hearings and Appeals ("OMHA") received a timely request for an Administrative Law Judge ("ALJ") hearing. The amount in controversy meets the jurisdictional requirements for a hearing before OMHA. An ALJ hearing was held on January 30, 2018, before the Honorable Jeffrey S. Gulin. The Enrollee was present and provided testimony. Dan McCoy and Dr. Ellen Wiegner, MD represented the Enrollee. Brian Macheath was present on behalf of the health plan. All the exhibits were admitted into the record.

ISSUES

1. Whether the Plan is required to pre-approve an Optune device.

FINDINGS OF FACT

1. The Enrollee is requesting the Plan to pre-approve an Optune device.
2. The surgical pathology biopsy report dated August 22, 2017, indicated the Enrollee's diagnosis was Glioblastoma multiforma, WHO grade 4. (Exh. 2, p. 3).
3. The office note from Mercy Cancer Institute of Greater Sacramento dated August 25, 2017, indicated the Beneficiary had a malignant neoplasm of parietal lobe. (Exh. 2, pp. 9-11).
4. The office note from Mercy Cancer Institute of Greater Sacramento dated September 7, 2017, indicated the Enrollee's biopsy showed glioblastoma multiform grade 4. Surgical resection was not recommended. (Exh. 2, pp. 4-8).
5. The office note from Mercy Cancer Institute of Greater Sacramento dated October 30, 2017, indicated the Enrollee's diagnosis was malignant neoplasm of parietal lobe diagnosed on September 27, 2017. The plan stated that Optune was approved, and will start about "2 weeks post RT," (Exh. 2, pp. 25-26).
6. The Optuno Prescription Form was signed and dated by the physician on October 23, 2017. It indicated the Enrollee's diagnosis was Glioblastoma. (Exh. 2, p. 1).
7. The physician letter dated November 27, 2017, indicates that the Enrollee, a 70-year-old male, was diagnosed with glioblastoma. He first presented to his primary care doctor on August 21, 2017, with complaints of headaches and decreased level of consciousness as well as some falling over the weekend. A head CT of the brain showed a mass with 8mm of midline shift. On August 22, 2017, the Enrollee underwent a brain biopsy of the right parietal occipital mass, and pathology showed glioblastoma multiform grade 4. Surgical resection was not recommended. The Enrollee received radiation with concurrent Temodar (temozolomide). (Exh. 1, pp. 16-18).
8. The NCCN Clinical Practice Guidelines 2016 in Oncology for "Central Nervous System Cancers," include Tumor Treatment Field Therapy (TTFT) treatment for recurrent glioblastoma. (Exh. 2, pp. 32-35).
9. Pursuant to the Food and Drug Administration ("FDA"), "Radiation therapy and cancer drugs can allow patients to live longer than if they had no treatment. Adding Optune to temozolomide can allow patients to live even longer than with temozolomide alone." https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034S013d.pdf

10. Pursuant to the NIH, "The Food and Drug Administration (FDA) of the United States approved TTF for recurrent GBM and newly diagnosed GBM in 2011 and 2015, respectively." <https://www.ncbi.nlm.nih.gov/m/pubmed/28841803/>
11. Pursuant to the National Institute of Health ("NIH"), "Glioblastoma (GBM) is the most common and aggressive malignant brain tumor in adults. Current treatment options at diagnosis are multimodal and include surgical resection, radiation, and chemotherapy. Significant advances in the understanding of the molecular pathology of GBM and associated cell signaling pathways have opened opportunities for new therapies for recurrent and newly diagnosed disease. Innovative treatments, such as tumor-treating fields (TTFields) [Optune] and immunotherapy, give hope for enhanced survival." <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5123811/>
12. NIH classifies glioblastoma multiform as a rare disease with limited treatment options. <https://rarediseases.info.nih.gov/diseases/2491/glioblastoma>
13. Pursuant to the American Association for Cancer Research, "Interim data from the first 315 patients enrolled in the trial led the U.S. Food and Drug Administration to approve the Optune medical device for newly diagnosed glioblastoma. "Now we are reporting the final results for all 695 patients enrolled on the trial, including long-term outcome. Our data firmly establish the survival benefit of treatment with TTFields," said Stupp. The median overall survival for patients randomly assigned TTFields and temozolomide was 21 months, compared with 16 months for those randomly assigned temozolomide alone. The two-, three-, four-, and five-year survival rates for patients who received TTFields and temozolomide were significantly improved compared with those for patients who received temozolomide alone: 43 percent versus 31 percent; 26 percent versus 16 percent; 20 percent versus 8 percent; and 13 percent versus 5 percent. TTFields showed an effect in all subgroups of patients treated, including the patients who have the most unfavorable prognostic factors." (April 2, 2017). <http://www.aacr.org/Newsroom/Pages/News-Release-Detail.aspx?ItemID=1029#.WntqoH1LnM>

LEGAL FRAMEWORK

A. Jurisdiction/Scope of Review/Standard of Review

OMHA has jurisdiction to hear appeals of QIC reconsiderations. 42 C.F.R. § 405.1002. The decision of the ALJ or attorney adjudicator on a request for hearing is binding on all parties unless the Medicare Appeals Council ("Council") reviews or the case is escalated to Federal district court. 42 C.F.R. § 405.1048. ALJ or attorney adjudicator decisions are reviewed by the Council in accordance with §§405.980, 405.1110, and 405.1138.

The issues before the ALJ or attorney adjudicator include all issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the appellant's favor. 42 C.F.R. § 405.1032(a). The ALJ or attorney adjudicator conducts a *de novo* review and issues a decision based on the record. 42 C.F.R. § 405.1000(d).

B. Statutes and Regulations

According to § 1862(a)(1)(A) of the Social Security Act ("Act"), Medicare may not make a payment under part A or part B for anything which is not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Section 1852(a) of the Act outlines the basic benefits in a case involving a Medicare Advantage ("MA") Organization and states in pertinent part:

(1) (A) In general.—Except as provided in section 1859(b)(3) for MSA plans and except as provided in paragraph (6) for MA regional plans, each Medicare+Choice plan shall provide to members enrolled under this part, through providers and other persons that meet the applicable requirements of this title and part A of title XI, benefits under the original Medicare fee-for-service program option (and, for plan years before 2006, additional benefits required under section 1854(f)(1)(A))

(B) Benefits under the original Medicare fee-for-service program option defined.—

(i) In general.—For purposes of this part, the term "benefits under the original Medicare fee-for-service program option" means those items and services (other than hospice care) for which benefits are available under parts A and B to individuals entitled to benefits under part A and enrolled under part B, with cost-sharing for those services as required under parts A and B or, subject to clause (iii), [418]an actuarially equivalent level cost-sharing as determined in this part.

The general regulations for Medicare Advantage Organizations are outlined in 42 C.F.R. § 422.100 which states "An MA organization must make timely and reasonable payment to or on behalf of the plan enrollee for the following services obtained from a provider or supplier that does not contract with the MA organization to provide services covered by the MA plan."

The requirements relating to basic benefits are outlined in 42 C.F.R. § 422.101. The guidelines for access to services for Medicare Advantage plan member are set out in 42 C.F.R. § 422.112. An MA organization is required to comply with CMS national coverage determinations, general coverage guidelines included in original Medicare manuals and instructions and the written coverage decisions of local Medicare contractors with jurisdiction for claims in the geographic area in which the services are covered under the MA plan. 42 C.F.R. § 422.101(b).

C. National Coverage Determination

A National Coverage Determination ("NCD"), if applicable, is binding on the ALJ. 42 C.F.R. § 405.1060(a)(4). There is no applicable NCD regarding the items at issue.

D. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by Centers for Medicare and Medicaid Services ("CMS"), no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. See also 42 C.F.R. §405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that establishes criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations ("LCDs"). Administrative Law Judges are not bound by LCDs, but will give substantial deference to these policies when applicable. 42 C.F.R. §405.1062. If an Administrative Law Judge does not follow a policy in a particular case, the Administrative Law Judge must explain why in the decision. 42 C.F.R. §405.1062.

The Contractor with jurisdiction over the Enrollee's geographical area has issued LCD L34823.

CMS issued the *Medicare Managed Care Manual ("MMCM") (Internet-Only Manual Pub'n 100-16)*, ch. 10, sets forth specific guidance regarding Medicare Advantages plans.

E. Evidence of Coverage

The Plan's Evidence of Coverage covers items and services in accordance with Medicare rules. (Exh. 3).

ANALYSIS

At issue, is whether the Plan should pre-approve an Optune device for the Enrollee.

Pursuant to LCD 34823, tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. The regulations direct an ALJ to give "substantial deference" to LCDs. 42 C.F.R. § 405.1062(a). However, the regulations also permit an ALJ to decline to follow a local coverage policy in an individual case. 42 C.F.R. § 405.1062(a). In this case, the undersigned does not give substantial deference to LCD L34823. The undersigned is not challenging the validity or substance of the LCD. This is based on the following unique facts of this case, that warrant policy should not be followed.

Research articles, FDA approval, and NIH studies support the conclusion that TTFT (Optune) is safe and effective in treating the Enrollee's diagnosis of Glioblastoma. The NIH identifies Glioblastoma as a rare disease with limited treatment options. <https://rarediseases.info.nih.gov/diseases/2491/glioblastoma>. The FDA approved TTF for recurrent GBM and newly diagnosed GBM in 2011 and 2015. <https://www.ncbi.nlm.nih.gov/pubmed/28841803/>. This reflects successful clinical trials where using Optune with temozolomide allowed patients to live even longer than with temozolomide alone.

On August 22, 2017, the Enrollee underwent a brain biopsy of the right parietal occipital mass, and pathology showed glioblastoma multiforme grade 4. (Exh. 1, pp. 16-18). Surgical resection was not recommended. *Id.* The Enrollee received radiation with concurrent Temodar (temozolomide). *Id.* Due to the nature of this rare disease, limited treatment options, and

favorable outcomes with TTFT, Optune is the best FDA approved option for treating his glioblastoma. Although, there is specific policy, LCD L34823, that would not allow Medicare coverage for Optune, the research provided and unique facts of this case demonstrate that there are other factors to consider here that outweigh the application of LCD L34823. Hence, based on the unique facts and medical research specific to this individual case, LCD L34823, should not be followed.

Here, the Optune device meets the requirements for Medicare coverage because the device has been shown to be reasonable and necessary for the treatment of glioblastoma multiform. The medical documentation provided indicates the FDA has approved Optune as being safe and effective for treating glioblastoma. Further, the documentation demonstrates that the use of Optune used consistent with FDA indication can be expected to provide a favorable outcome and higher quality of life for the Enrollee. Therefore, the Plan should pre-approve the Optune device for the Enrollee.

CONCLUSIONS OF LAW

The requested Optune device is medically needed for the Enrollee. The Plan does have to pre-approve the Optune device.

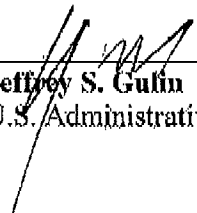
ORDER

For the reasons discussed above the Medicare Advantage Organization is directed to process the claim in accordance with this decision.

SO ORDERED:

FEB - 8 2018

Dated: _____



Jeffrey S. Gulin
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Arlington Field Office
Arlington, Virginia

Appellant:	ALJ Appeal No.: 1-7901539421
Beneficiary:	Medicare Part B
HICN:	Before: Jeffrey S. Gulin U.S. Administrative Law Judge

DECISION

After considering the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is entered for the Appellant/Beneficiary.

PROCEDURAL HISTORY

("Appellant/Beneficiary") seeks coverage for Elec Stim Cancer Treatment (E0766) provided on November 9, 2017, December 9, 2017, and January 9, 2018 ("the Dates of Service"). (Exh. 1, p. 3). The Medicare Administrative Contractor ("MAC"), denied coverage initially and on redetermination. Following the denial, the Appellant requested reconsideration from a Qualified Independent Contractor ("QIC"). On August 17, 2018, the QIC issued an unfavorable reconsideration decision. (Exh. 1, p. 1). According to the reconsideration decision, the LCD states tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. The DME MAC denied payment because tumor treatment field therapy or therapy supplies were not covered by Medicare, as the currently published studies in the medical literature did not clearly document the effectiveness of the device. The QIC upheld the denial and found the LCD requirements have not been met. (Exh. 1, p. 4). The QIC determined an Advance Beneficiary Notice ("ABN") was not issued and found the Provider, Novocure, Inc., liable for the non-covered amount. (Exh. 1, p. 5).

On September 24, 2018, the Office of Medicare Hearings and Appeals ("OMHA") received the Appellant's request for review by an Administrative Law Judge ("ALJ"). (Exh. 3, p. 1). The amount in controversy meets the statutorily required amount for an ALJ hearing. Judge Jeffrey S. Gulin held a telephone conference hearing on October 31, 2018. Attorney Debra Parrish provided argument and Ms. Julie Miles, RN, BSN, and CEN, was sworn in and provided testimony and/or argument for the Appellant. There were no objections and all exhibits were admitted into the record. (Hearing CD).

ISSUES

1. Whether the Elec Stim Cancer Treatment (E0766) provided to the Beneficiary on the dates of service meet Medicare coverage criteria.
2. Whether the services provided are medically necessary under Section 1862(a)(1)(A) of the Social Security Act (“Act”) and covered under Medicare.
3. If the services are found to be excluded from coverage under Section 1862(a)(1)(A), then another issue to be determined is whether payment may nevertheless be made to appellant under the limitation on liability provisions of Section 1879 of the Act.

FINDINGS OF FACT

1. The Beneficiary/Appellant is seeking Medicare coverage for Elec Stim Cancer Treatment (E0766) provided on the dates of service. (Exh. 1, p. 3).
2. The 28-year-old Beneficiary underwent total gross removal of a glioblastoma with chemo radiation. The diagnosis included brain lesion excision and glioblastoma. (Exh. 2, p. 64).
3. Assessment of need shows Optune would be administered in the home. (Exh. 2, p. 17). Optune treatment was ordered by the attending physician on October 30, 2012 for 6 months and the Appellant had already been using the treatment. (Exh. 2, p. 13).
4. During a radiation oncology follow-up from January 4, 2018, the Beneficiary demonstrated reasonably good compliance with Optune. (Exh. 2, p. 34). The array was in place for further treatment and no significant skin irritation was present. (Exh. 2, p. 36). The attending physician ordered continued Optune administration on January 4, 2018 for 6 months. (Exh. 2, p. 12).
5. The Appellant received bills for the treatments on November 9, 2017, December 9, 2017, and January 9, 2018. (Exh. 2, pp. 1, 2, 3).
6. An article included from NovoCure with the product dossier describes Food and Drug Administration (“FDA”) approval for treatment of recurrent glioblastoma Mutiforme. (Exh. 2, p. 113). The FDA gave premarket approval (“PMA”) for the device in 2011. (Exh. 2, p. 119).
7. A study published in the 2015 Journal of the American Medical Association (“JAMA”) edition entitled “Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma – A Randomized Clinical Trial” found in the interim analysis of 315 patients with glioblastoma who completed standard chemo radiation therapy, adding TTFields to maintenance temozolomide chemotherapy significantly prolonged progress-free and overall survival. (Exh. 2, p. 71).
8. Electric field therapy is included in the National Comprehensive Care Network (“NCCN”) guidelines for treatment with standard brain radiation therapy for central nervous system cancers for 2016. (Exh.1, pp. 87, 88). A letter from the Appellant’s

representative and attorney states the Beneficiary was diagnosed with glioblastoma in February 2015. (Exh. 3, p. 1). The FDA deemed it unethical to withhold TTFT from those not receiving it during the clinical trial and ordered the sponsor to discontinue the study. (Exh. 3, pp. 1-2). This was the first time the FDA stopped a brain tumor study. (Exh. 3, p. 1).

LEGAL FRAMEWORK

A. Jurisdiction/Scope of Review/Standard of Review

OMHA has jurisdiction to hear appeals of QIC reconsiderations. 42 C.F.R. § 405.1002. ALJ decisions bind parties unless the Medicare Appeals Council (“Council”) reviews or the case is escalated to Federal district court. 42 C.F.R. § 405.1048. ALJ decisions are reviewed by the Council in accordance with §§ 405.980, 405.1110, and 405.1138.

The issues before the ALJ include issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the appellant’s favor. 42 C.F.R. § 405.1032(a). The ALJ conducts *de novo* review and issues a decision based on the record. 42 C.F.R. § 405.1000(d).

PRINCIPLES OF LAW

A. Statutes and Regulations

Section 1831 establishes the Supplemental Medical Insurance Program for the aged and disabled under Medicare Part B. Section 1832 establishes the scope of benefits that are provided to beneficiaries under the Medicare Part B insurance program. Under § 1832(a)(2)(B), an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with them made by a provider of services. (*See also* 42 CFR § 410.3). Section 1833(e) provides that “[n]o payment shall be made to any provider of services . . . unless there has been furnished such information as may be necessary in order to determine the amounts due such provider” (*See also* 42 CFR § 424.5(a)(6)).

Section 1862(a)(1)(A) of Title XVIII of the Social Security Act (SSA) excludes expenses incurred for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Section 1861(s)(6) defines the term “medical and other health services.” (*See also* 42 CFR § 410.10(h)). Also considered is 42 CFR § 414.200-232 implementing §§ 1834 (a) and (h) of the Act by specifying how payments are made for the purchase or rental of new and used durable medical equipment and prosthetic and orthotic devices for Medicare beneficiaries. Section 1862(a)(1)(A) provides that notwithstanding any other provision of the Act, no payment shall be made for any expenses incurred for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. (*See also* 42 CFR § 411.15(k)).

The Centers for Medicare & Medicaid Services (CMS), the federal agency that administers the Medicare program, has established a coding system for screening, processing, identifying, and paying Medicare claims—the Healthcare Common Procedure Coding System (HCPCS). The HCPCS incorporates codes developed by the American Medical Association, Current Procedure Terminology (CPT) codes, to identify and describe medical services and items. (See 42 C.F.R. §§ 414.2, 414.40).

B. National Coverage Determinations

A National Coverage Determination (“NCD”), if applicable, is binding on the ALJ. 42 C.F.R. §405.1060(a)(4).

C. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by Centers for Medicare and Medicaid Services (“CMS”), no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. See also 42 C.F.R. §405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that establishes criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (“LCDs”). Administrative Law Judges are not bound by LCDs, but will give substantial deference to these policies when applicable. If an Administrative Law Judge does not follow a policy in a particular case, the Administrative Law Judge must explain why in the decision. 42 C.F.R. §405.1062.

When a NCD or LCD or other directives are lacking, the adjudication process requires the Judge to determine coverage by performing the same review that Medicare contractors, according to the Medicare Program Integrity Manual (Publ. 100-08), Chapter 13.7.1, would perform when developing a LCD.

Contractor LCDs shall be based on the strongest evidence available. The extent and quality of supporting evidence is key to defending challenges to LCDs. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on:

- Published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and
- General acceptance by the medical community (standard of practice), as supported by sound medical evidence based on:
- Scientific data or research studies published in peer-reviewed medical journals;
- Consensus of expert medical opinion (i.e., recognized authorities in the field: or

- Medical opinion derived from consultations with medical associations or other health care experts.

Local Coverage Determination L34823 entitled “Tumor Treatment Field Therapy” provides coverage guidance in this case: Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. Policy Article A52711 provides further guidance by stating “in order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met.”

ANALYSIS

The QIC issued an unfavorable reconsideration decision. (Exh. 1, p. 1). According to the reconsideration decision, the LCD states tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. The DME MAC denied payment because tumor treatment field therapy or therapy supplies were not covered by Medicare, as the currently published studies in the medical literature did not clearly document the effectiveness of the device. The QIC upheld the denial and found the LCD requirements have not been met. (Exh. 1, p. 4). An Advance Beneficiary Notice (“ABN”) was not issued and found the Provider, Novocure, Inc., liable for the non-covered amount. (Exh. 1, p. 5).

Local Coverage Determination L34823 entitled “Tumor Treatment Field Therapy” provides coverage guidance in this case: Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. National Government Services, Inc. Local Coverage Determination L34823: Tumor Treatment Field Therapy (“TTFT”) (L34823) (October 2017). Policy Article A52711 provides further guidance by stating “in order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met.” Also, administrative law judges are not bound by LCDs, but will give substantial deference to these policies when applicable. If an administrative law judge does not follow a policy in a particular case, the administrative law judge must explain why in the decision. 42 C.F.R. §405.1062.

Attorney Debra Parrish stated Medicare has issued new regulations for how LCDs need to be developed and an advisory committee should be created by 2019. The claim was denied for lack of clinical effectiveness. But, the clinical trial shows the effectiveness because it was terminated early and deemed unethical to withhold treatment from individuals with the condition. It is hard to imagine a more effective result. This was the first time the FDA shut down a brain tumor study for positive results. The statement suggesting lack of effectiveness completely flies in the face of the evidence. Nurse Miles confirmed the glioblastoma diagnosis. The NCCN give suggested guidelines for patients to follow and he followed the criteria. He had a resection, completed chemo radiation, and continued with maintenance temozolomide and Optune and has been progression free since. The treatment was medically reasonable and necessary based on the medical record. (Hearing CD).

The Medicare coverage requirements are met. The 28-year-old Beneficiary underwent total gross removal of a glioblastoma with chemo radiation. The diagnosis included brain lesion excision and glioblastoma. (Exh. 2, p. 64). The attending physician ordered Optune on October 30, 2017 and January 4, 2018 and the Beneficiary received the treatment on November 9, 2017, December

9, 2017, and January 9, 2018. (Exh. 2, pp. 1, 2, 3, 12, 13). Administrative law judges are not bound by LCDs, but must provide substantial deference. If an LCD is not followed, the ALJ must explain why in the decision. 42 C.F.R. §405.1062. In this case, the undersigned declines to follow the LCD while also providing substantial deference. As described above, local coverage determination (“LCD”) L34823 finds the TTFT not medically reasonable and necessary. But, studies from the FDA and new literature from the medical community since the LCD was first issued show the treatment is beneficial to patients such as the Appellant and is medically reasonable and necessary. Examining the process for how contractors make coverage determinations is helpful in establishing medical necessity for the service outside the determination. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on general acceptance by the medical community (standard of practice), as supported by sound medical evidence based on scientific data or research studies published in peer-reviewed medical journals, consensus of expert medical opinion (i.e., recognized authorities in the field; or medical opinion derived from consultations with medical associations or other health care experts. MPIM ch. 13 § 7.1. General acceptance in the medical community is supported by sound evidence based on scientific data or research studies. Optune is approved by the FDA for recurrent glioblastoma Mutiforme. (Exh. 2, p. 113). The FDA discontinuing the initial study for those not receiving it suggests treatment was medically necessary for the entire group based on scientific data. (Exh. 3, pp. 1-2). Also, a general acceptance in the medical community is documented by electric field therapy inclusion in the NCCN guidelines for treatment with standard brain radiation therapy. (Exh.1, pp. 87, 88). Finally, sound medical evidence is further shown in the study published by the Journal of the American Medical Association (“JAMA”) finding adding TTFields to maintenance chemotherapy significantly prolonged progress-free and overall survival. Medical opinion derived from consultations with a medical association is also shown by the study. (Exh. 2, p. 71). The Appellant was diagnosed with glioblastoma and benefited from the Optune treatment. The QIC determined the record does not show effectiveness. (Exh. 1, p. 4). But, effectiveness is shown by the FDA discontinuing the study as described and the Appellant’s treatment following guidelines published by the NCCN. (Hearing CD). The Appellant/Beneficiary was diagnosed with glioblastoma and the treatment stopped progression. The Medicare coverage requirements are met for the treatment Optune treatment on the dates of service.

The service is medically reasonable and necessary under Section 1862(a)(1)(A) of the Social Security Act. The Appellant is entitled to Medicare coverage for the Elec Stim Cancer Treatment (E0766) provided on the dates of service.

CONCLUSIONS OF LAW

Accordingly and after careful consideration, there is sufficient evidence supporting the Elec Stim Cancer Treatment (E0766) provided on the dates of service meets Medicare coverage criteria. The service was medically reasonable and necessary as required by Section 1862(a)(1)(A) of the Act and the Appellant is entitled to Medicare coverage.

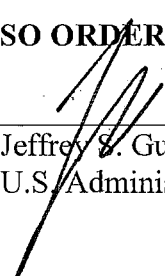
ORDER

The Medicare Contractor is **DIRECTED** to process the appeal in accordance with this decision.

NOV - 7 2018

Dated: _____

SO ORDERED.



Jeffrey S. Gulin
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Arlington Field Office
Arlington, Virginia

Appellant:	ALJ Appeal No.: 1-7835229465
Beneficiary:	Medicare Part B
HICN:	Before: Jeffrey S. Gulin U.S. Administrative Law Judge

DECISION

After considering the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is entered for the Appellant/Beneficiary.

PROCEDURAL HISTORY

Mrs. (“Appellant/Beneficiary”) seeks coverage for Elec Stim Cancer Treatment (E0766) provided on September 14, 2017, October 14, 2017, and November 14, 2017 (“the Dates of Service”). (Exh. 1, p. 3). Noridian, the Medicare Administrative Contractor (“MAC”), denied coverage initially and on redetermination. (Exh. 1, p. 8). Following the denial, the Appellant requested reconsideration from a Qualified Independent Contractor (“QIC”). On August 3, 2018, the QIC determined the local coverage determination states tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. In this instance, the submitted documentation indicates the Beneficiary has a diagnosis of glioblastoma multiform involving the left occipital lobe. However, the medical documentation does not support the need for the device. There is insufficient documentation to quantify the effects of the device. The currently published studies in the medical literature do not clearly document the effectiveness of this device. As such, payment cannot be allowed. Based on available documentation, the requirements of the LCD have not been met. (Exh. 1, p. 4). The QIC determined an Advance Beneficiary Notice (“ABN”) was not issued and found the Provider liable. (Exh. 1, p. 5).

On August 27, 2018, the Office of Medicare Hearings and Appeals (“OMHA”) received the Appellant’s request for review by an Administrative Law Judge (“ALJ”). (Exh. 3, p. 1). The amount in controversy meets the statutorily required amount for an ALJ hearing. Judge Jeffrey S. Gulin held a telephone conference hearing on October 17, 2018. Attorney Bridget Noonan provided testimony and/or argument for the Appellant and Mr. Dan McCoy, Case Manager, NovoCure, Inc., served as a witness and was sworn in and provided testimony and/or argument. There were no objections and all exhibits were admitted into the record. (Hearing CD).

ISSUES

1. Whether the Elec Stim Cancer Treatment (E0766) provided to the Beneficiary on the dates of service meet Medicare coverage criteria.
2. Whether the services provided are medically necessary under Section 1862(a)(1)(A) of the Social Security Act (“Act”) and covered under Medicare.
3. If the services are found to be excluded from coverage under Section 1862(a)(1)(A), then another issue to be determined is whether payment may nevertheless be made to appellant under the limitation on liability provisions of Section 1879 of the Act.

FINDINGS OF FACT

1. The Beneficiary/Appellant is seeking Medicare coverage for Elec Stim Cancer Treatment (E0766) provided on the dates of service. (Exh. 1, p. 53).
2. The Beneficiary was diagnosed with glioblastoma multiform in 2011. (Exh. 2, pp. 1, 25). The attending physician sought coverage for Optune for the Beneficiary with newly diagnosed glioblastoma. (Exh. 2, p. 4). Optune was prescribed by the attending physician on April 28, 2017 for 6 months. (Exh. 2, p. 2). The treatment was again prescribed on October 10, 2017 for another 6 months. (Exh. 2, p. 1).
3. Assessment of need and the agreement with Novocure indicate the treatment would be administered in the home. (Exh. 2, pp. 6, 8).
4. An article included from NovoCure with the product dossier describes Food and Drug Administration (“FDA”) approval for treatment of recurrent glioblastoma multiforme. (Exh. 2, p. 94). The FDA gave premarket approval (“PMA”) for the device in 2011. (Exh. 2, p. 89).
5. A study published in the 2015 Journal of the American Medical Association (“JAMA”) edition entitled “Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma – A Randomized Clinical Trial” found in the interim analysis of 315 patients with glioblastoma who completed standard chemo radiation therapy, adding TTFields to maintenance temozolomide chemotherapy significantly prolonged progress-free and overall survival. (Exh. 1, p. 92).
6. Electric field therapy is included in the National Comprehensive Care Network (“NCCN”) guidelines for treatment with standard brain radiation therapy for central nervous system cancers for 2016. (Exh.1, pp. 87, 88). A letter from the Appellant’s representative and attorney states the FDA deemed it unethical to withhold TTFT from those not receiving it during the clinical trial and ordered the sponsor to discontinue the study. This was the first time the FDA stopped a brain tumor study. (Exh. 3, p. 1).

LEGAL FRAMEWORK

A. Jurisdiction/Scope of Review/Standard of Review

OMHA has jurisdiction to hear appeals of QIC reconsiderations. 42 C.F.R. § 405.1002. ALJ decisions bind parties unless the Medicare Appeals Council (“Council”) reviews or the case is escalated to Federal district court. 42 C.F.R. § 405.1048. ALJ decisions are reviewed by the Council in accordance with §§ 405.980, 405.1110, and 405.1138.

The issues before the ALJ include issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the appellant’s favor. 42 C.F.R. § 405.1032(a). The ALJ conducts *de novo* review and issues a decision based on the record. 42 C.F.R. § 405.1000(d).

PRINCIPLES OF LAW

A. Statutes and Regulations

Section 1831 establishes the Supplemental Medical Insurance Program for the aged and disabled under Medicare Part B. Section 1832 establishes the scope of benefits that are provided to beneficiaries under the Medicare Part B insurance program. Under § 1832(a)(2)(B), an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with them made by a provider of services. (*See also* 42 CFR § 410.3). Section 1833(e) provides that “[n]o payment shall be made to any provider of services . . . unless there has been furnished such information as may be necessary in order to determine the amounts due such provider” (*See also* 42 CFR § 424.5(a)(6)).

Section 1862(a)(1)(A) of Title XVIII of the Social Security Act (SSA) excludes expenses incurred for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Section 1861(s)(6) defines the term “medical and other health services.” (*See also* 42 CFR § 410.10(h)). Also considered is 42 CFR § 414.200-232 implementing §§ 1834 (a) and (h) of the Act by specifying how payments are made for the purchase or rental of new and used durable medical equipment and prosthetic and orthotic devices for Medicare beneficiaries. Section 1862(a)(1)(A) provides that notwithstanding any other provision of the Act, no payment shall be made for any expenses incurred for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. (*See also* 42 CFR § 411.15(k)).

The Centers for Medicare & Medicaid Services (CMS), the federal agency that administers the Medicare program, has established a coding system for screening, processing, identifying, and paying Medicare claims—the Healthcare Common Procedure Coding System (HCPCS). The HCPCS incorporates codes developed by the American Medical Association, Current Procedure Terminology (CPT) codes, to identify and describe medical services and items. (*See* 42 C.F.R. §§ 414.2, 414.40).

B. National Coverage Determinations

A National Coverage Determination (“NCD”), if applicable, is binding on the ALJ. 42 C.F.R. §405.1060(a)(4).

C. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by Centers for Medicare and Medicaid Services (“CMS”), no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. See also 42 C.F.R. §405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that establishes criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (“LCDs”). Administrative Law Judges are not bound by LCDs, but will give substantial deference to these policies when applicable. If an Administrative Law Judge does not follow a policy in a particular case, the Administrative Law Judge must explain why in the decision. 42 C.F.R. §405.1062.

When a NCD or LCD or other directives are lacking, the adjudication process requires the Judge to determine coverage by performing the same review that Medicare contractors, according to the Medicare Program Integrity Manual (Publ. 100-08), Chapter 13.7.1, would perform when developing a LCD.

Contractor LCDs shall be based on the strongest evidence available. The extent and quality of supporting evidence is key to defending challenges to LCDs. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on:

- Published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and
- General acceptance by the medical community (standard of practice), as supported by sound medical evidence based on:
- Scientific data or research studies published in peer-reviewed medical journals;
- Consensus of expert medical opinion (i.e., recognized authorities in the field: or
- Medical opinion derived from consultations with medical associations or other health care experts.

Local Coverage Determination L34823 entitled “Tumor Treatment Field Therapy” provides coverage guidance in this case: Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. Policy Article A52711 provides further guidance by stating “in order

for a beneficiary's equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met."

ANALYSIS

The QIC determined the local coverage determination states tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. In this instance, the submitted documentation indicates the Beneficiary has a diagnosis of glioblastoma multiform involving the left occipital lobe. However, the medical documentation does not support the need for the device. There is insufficient documentation to quantify the effects of the device. The currently published studies in the medical literature do not clearly document the effectiveness of this device. As such, payment cannot be allowed. Based on available documentation, the requirements of the LCD have not been met. (Exh. 1, p. 4). The QIC determined an Advance Beneficiary Notice ("ABN") was not issued and the Provider was found liable. (Exh. 1, p. 5).

Local Coverage Determination L34823 entitled "Tumor Treatment Field Therapy" provides coverage guidance in this case: Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. National Government Services, Inc. Local Coverage Determination L34823: Tumor Treatment Field Therapy ("TTFT") (L34823) (October 2017). Policy Article A52711 provides further guidance by stating "in order for a beneficiary's equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met." Also, administrative law judges are not bound by LCDs, but will give substantial deference to these policies when applicable. If an administrative law judge does not follow a policy in a particular case, the administrative law judge must explain why in the decision. 42 C.F.R. §405.1062.

Attorney Noonan states the Optune System is the subject of an LCD reconsideration request. In response to the request, the DME MAC medical directors sent a letter stating the LCD does not apply to cases with newly diagnosed glioblastoma. The Appellant is a newly diagnosed patient for the dates of service at issue. There is no district court decision on the coverage of the device and the medical directors do not believe the LCDs apply in the new cases. Also, the QIC denied because effectiveness could not be quantified. But, this is not a requirement for Medicare coverage. Even so, the Beneficiary has been alive for over 7 years since the diagnosis. Mr. McCoy, Case Manager for Novocure, Inc., testified and argued, in relevant part how no response has been received yet for the request made to contractors to reconsider the LCD to cover the service. He also testified the Appellant has been using the device for 7 years. (Hearing CD).

The Medicare coverage requirements are met. The Beneficiary was diagnosed with glioblastoma multiform in 2011. (Exh. 2, pp. 1, 25). The attending physician sought coverage for Optune for the Beneficiary with newly diagnosed glioblastoma and prescriptions cover the dates of service. (Exh. 2, pp. 1, 2, 4). Assessment of need and the agreement with Novocure indicate the treatment would be administered in the home under Part B rather than under an inpatient Part A admission. (Exh. 2, pp. 6, 8). Administrative law judges are not bound by LCDs, but must provide substantial deference. If an LCD is not followed, the ALJ must explain why in the decision. 42 C.F.R. §405.1062. In this case, the undersigned declines to follow the LCD while also providing substantial deference. As described above, local coverage determination ("LCD") L34823 finds the TTFT not medically reasonable and necessary. But, studies from the FDA and new literature from the medical community since the LCD was first issued show the treatment is beneficial to patients such as the Appellant and is medically reasonable and necessary. Examining the process

for how contractors make coverage determinations is helpful in establishing medical necessity for the service outside the determination. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on general acceptance by the medical community (standard of practice), as supported by sound medical evidence based on scientific data or research studies published in peer-reviewed medical journals, consensus of expert medical opinion (i.e., recognized authorities in the field: or medical opinion derived from consultations with medical associations or other health care experts. MPIM ch. 13 § 7.1. General acceptance in the medical community is supported by sound medical evidence based on scientific data or research studies. Optune is approved by the FDA for recurrent glioblastoma multiforme. (Exh. 2, p. 94). The FDA discontinuing the initial study for those not receiving it suggests the treatment was medically necessary for the entire group based on scientific data. (Exh. 3, p. 1). Also, a general acceptance in the medical community is documented by electric field therapy inclusion in the NCCN guidelines for treatment with standard brain radiation therapy. (Exh.1, p. 88). Finally, sound medical evidence is further shown in the study published by the Journal of the American Medical Association ("JAMA") finding adding TTFIELDS to maintenance chemotherapy significantly prolonged progress-free and overall survival. Medical opinion derived from consultations with a medical association is also shown by the study. (Exh. 1, p. 92). The Appellant has been using the treatment at issue for 7 years and Optune is subject to an LCD reconsideration request. Further, the DME MAC medical directors state the applicable LCD does not apply to newly formed glioblastoma like the Appellant's. (Hearing CD). The undersigned departs from the LCD because there is evidence showing acceptance and use in the medical community for the diagnosis at issue as documented by studies and articles in the record. The Appellant/Beneficiary was diagnosed with glioblastoma multiforme and the treatment received is supported by the included guidance. Taking the prior into consideration, the Medicare coverage requirements are met for the dates of service.

The service is medically reasonable and necessary under Section 1862(a)(1)(A) of the Social Security Act. The Appellant is entitled to Medicare coverage for the Elec Stim Cancer Treatment (E0766) provided on the dates of service.

CONCLUSIONS OF LAW

Accordingly and after careful consideration, there is sufficient evidence supporting the Elec Stim Cancer Treatment (E0766) provided on the dates of service meets Medicare coverage criteria. The service was medically reasonable and necessary as required by Section 1862(a)(1)(A) of the Act and the Appellant is entitled to Medicare coverage.

ORDER

The Medicare Contractor is **DIRECTED** to process the appeal in accordance with this decision.

NOV - 7 2018

Dated: _____

SO ORDERED.

Jeffrey S. Gulin
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Arlington Field Office
Arlington, Virginia

Appellant:	ALJ Appeal No.: 1-7865202111
Beneficiary:	Medicare Part B
HICN:	Before: Jeffrey S. Gulin U.S. Administrative Law Judge

DECISION

After considering the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is entered for the Appellant/Beneficiary.

PROCEDURAL HISTORY

("Appellant/Beneficiary") seeks coverage for Elec Stim Cancer Treatment (E0766) provided on September 5, 2017, October 5, 2017, and November 5, 2017 ("the Dates of Service"). (Exh. 1, p. 3). The Medicare Administrative Contractor ("MAC") denied coverage initially and on redetermination. Following the denial, the Appellant requested reconsideration from a Qualified Independent Contractor ("QIC"). On August 2, 2018, the QIC issued an unfavorable reconsideration decision. (Exh. 1, p. 1). The records do not support the device as reasonable and necessary, as required by local coverage determination ("LCD") L34823. The published studies in the medical literature do not clearly document the effectiveness of this device. If the Novocure TTF is denied as not reasonable and necessary, the corresponding transducer arrays will be denied as not reasonable and necessary and payment cannot be allowed. Based on the available documentation, the requirements of LCD L34823 have not been met. (Exh. 1, p. 4). The QIC determined an Advance Beneficiary Notice ("ABN") was not issued and found the Provider, Novocure, Inc., liable for the non-covered amount. (Exh. 1, p. 5).

On August 22, 2018, the Office of Medicare Hearings and Appeals ("OMHA") received the Appellant's request for review by an Administrative Law Judge ("ALJ"). (Exh. 3, p. 1). The amount in controversy meets the statutorily required amount for an ALJ hearing. Judge Jeffrey S. Gulin held a telephone conference hearing on December 20, 2018. Attorney Debra Parrish provided argument and Mr. Tim Parks, Registered Nurse ("RN"), of Novocure, Inc., was sworn in and provided testimony and/or argument for the Appellant. There were no objections and all exhibits were admitted into the record. (Hearing CD).

ISSUES

1. Whether the Elec Stim Cancer Treatment (E0766) provided to the Beneficiary on the dates of service meet Medicare coverage criteria.
2. Whether the services provided are medically necessary under Section 1862(a)(1)(A) of the Social Security Act (“Act”) and covered under Medicare.
3. If the services are found to be excluded from coverage under Section 1862(a)(1)(A), then another issue to be determined is whether payment may nevertheless be made to appellant under the limitation on liability provisions of Section 1879 of the Act.

FINDINGS OF FACT

1. The Beneficiary/Appellant is seeking Medicare coverage for Elec Stim Cancer Treatment (E0766) provided on the dates of service. (Exh. 1, p. 3).
2. The Beneficiary was diagnosed with right frontal lobe glioblastoma and received Temozolomide at 150 milligrams 5 times a day repeated every 28 days with Optune. (Exh. 2, p. 26).
3. The attending physician prescribed Optune on August 3, 2016. (Exh. 2, p. 8). An assessment of need form shows she would administer treatment with the device in the home. (Exh. 2, p. 9). The device was initially delivered on October 5, 2016. (Exh. 2, p. 21). She received bills for service dates on September 5, 2017, October 5, 2017, and November 5, 2017. (Exh. 2, pp. 1, 2, 3). An invoice from Novocure is included for TTF therapy and transducers. (Exh. 2, p. 4).
4. An article included from NovoCure with the product dossier describes Food and Drug Administration (“FDA”) approval for treatment of recurrent glioblastoma mutiforme. (Exh. 2, p. 78). The FDA gave premarket approval (“PMA”) for the device in 2011. (Exh. 2, p. 84).
5. A study published in the 2015 Journal of the American Medical Association (“JAMA”) edition entitled “Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma – A Randomized Clinical Trial” found in the interim analysis of 315 patients with glioblastoma who completed standard chemo radiation therapy, adding TTFields to maintenance Temozolomide chemotherapy significantly prolonged progress-free and overall survival. (Exh. 2, p. 43).
6. An article published in in BioMed Central found TTFields alone and in combination with chemotherapeutic agents effectively reduce the viability of MDR cell sub-lines that over-express ABC transporters. (Exh. 2, p. 164). Study results support chemo/TTFields combinations are expected to provide the same or even greater therapeutic efficacy with much lower drug concentrations and lower further overall toxicity. (Exh. 2, p. 181).
7. Electric field therapy is included in the National Comprehensive Care Network (“NCCN”) guidelines for treatment with standard brain radiation therapy for central

nervous system cancers for 2016. (Exh.2, pp. 31, 32). The appellant was diagnosed with glioblastoma in April of 2016 and has been treated with radiation and chemotherapy and the clinician prescribed TTFT. In 2013, TTFT was FDA approved and the administration deemed it unethical to withhold TTFT from those not receiving it during the clinical trial and ordered the sponsor to discontinue the study. This was the first time the FDA stopped a brain tumor study. (Exh. 3, p. 14).

LEGAL FRAMEWORK

A. Jurisdiction/Scope of Review/Standard of Review

OMHA has jurisdiction to hear appeals of QIC reconsiderations. 42 C.F.R. § 405.1002. ALJ decisions bind parties unless the Medicare Appeals Council (“Council”) reviews or the case is escalated to Federal district court. 42 C.F.R. § 405.1048. ALJ decisions are reviewed by the Council in accordance with §§ 405.980, 405.1110, and 405.1138.

The issues before the ALJ include issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the appellant’s favor. 42 C.F.R. § 405.1032(a). The ALJ conducts *de novo* review and issues a decision based on the record. 42 C.F.R. § 405.1000(d).

PRINCIPLES OF LAW

A. Statutes and Regulations

Section 1831 establishes the Supplemental Medical Insurance Program for the aged and disabled under Medicare Part B. Section 1832 establishes the scope of benefits that are provided to beneficiaries under the Medicare Part B insurance program. Under § 1832(a)(2)(B), an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with them made by a provider of services. (*See also* 42 CFR § 410.3). Section 1833(e) provides that “[n]o payment shall be made to any provider of services . . . unless there has been furnished such information as may be necessary in order to determine the amounts due such provider” (*See also* 42 CFR § 424.5(a)(6)).

Section 1862(a)(1)(A) of Title XVIII of the Social Security Act (SSA) excludes expenses incurred for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Section 1861(s)(6) defines the term “medical and other health services.” (*See also* 42 CFR § 410.10(h)). Also considered is 42 CFR § 414.200-232 implementing §§ 1834 (a) and (h) of the Act by specifying how payments are made for the purchase or rental of new and used durable medical equipment and prosthetic and orthotic devices for Medicare beneficiaries. Section 1862(a)(1)(A) provides that notwithstanding any other provision of the Act, no payment shall be made for any expenses incurred for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. (*See also* 42 CFR § 411.15(k)).

The Centers for Medicare & Medicaid Services (CMS), the federal agency that administers the Medicare program, has established a coding system for screening, processing, identifying, and paying Medicare claims—the Healthcare Common Procedure Coding System (HCPCS). The HCPCS incorporates codes developed by the American Medical Association, Current Procedure Terminology (CPT) codes, to identify and describe medical services and items. (See 42 C.F.R. §§ 414.2, 414.40).

B. National Coverage Determinations

A National Coverage Determination (“NCD”), if applicable, is binding on the ALJ. 42 C.F.R. §405.1060(a)(4).

C. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by Centers for Medicare and Medicaid Services (“CMS”), no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. See also 42 C.F.R. §405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that establishes criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (“LCDs”). Administrative Law Judges are not bound by LCDs, but will give substantial deference to these policies when applicable. If an Administrative Law Judge does not follow a policy in a particular case, the Administrative Law Judge must explain why in the decision. 42 C.F.R. §405.1062.

When a NCD or LCD or other directives are lacking, the adjudication process requires the Judge to determine coverage by performing the same review that Medicare contractors, according to the Medicare Program Integrity Manual (Publ. 100-08), Chapter 13.7.1, would perform when developing a LCD.

Contractor LCDs shall be based on the strongest evidence available. The extent and quality of supporting evidence is key to defending challenges to LCDs. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on:

- Published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and
- General acceptance by the medical community (standard of practice), as supported by sound medical evidence based on:
- Scientific data or research studies published in peer-reviewed medical journals;
- Consensus of expert medical opinion (i.e., recognized authorities in the field: or

- Medical opinion derived from consultations with medical associations or other health care experts.

Local Coverage Determination L34823 entitled “Tumor Treatment Field Therapy” provides coverage guidance in this case: Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. Policy Article A52711 provides further guidance by stating “in order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met.”

ANALYSIS

The Beneficiary/Appellant is seeking Medicare coverage for Elec Stim Cancer Treatment (E0766) provided on the dates of service. (Exh. 1, p. 3). According to the reconsideration decision, the records do not support the device as reasonable and necessary, as required by local coverage determination (“LCD”) L34823. The published studies in the medical literature do not clearly document the effectiveness of this device. If the Novocure TTF is denied as not reasonable and necessary, the corresponding transducer arrays will be denied as not reasonable and necessary and payment cannot be allowed. Based on the available documentation, the requirements of LCD L34823 have not been met. (Exh. 1, p. 4). The QIC determined an Advance Beneficiary Notice (“ABN”) was not issued and found the Provider, Novocure, Inc., liable for the non-covered amount. (Exh. 1, p. 5).

Local Coverage Determination L34823 entitled “Tumor Treatment Field Therapy” provides coverage guidance in this case: Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. National Government Services, Inc. Local Coverage Determination L34823: Tumor Treatment Field Therapy (“TTFT”) (L34823) (October 2017). Policy Article A52711 provides further guidance by stating “in order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met.” Also, administrative law judges are not bound by LCDs, but will give substantial deference to these policies when applicable. If an administrative law judge does not follow a policy in a particular case, the administrative law judge must explain why in the decision. 42 C.F.R. §405.1062.

Attorney Debra Parrish argued, in relevant part, how the 66-year-old Medicare beneficiary was diagnosed in April of 2016 with glioblastoma. She was then prescribed the Optune device consistent with the standard of care and the QIC denied the claim because literature does not document effectiveness. The literature is the opposite and demonstrates the effectiveness and the study was terminated during the interim analysis portion. The JAMA paper discusses the early termination because the results were so impressive and profound it was considered unethical to withhold treatment. JAMA is one of the top five journals in the country in terms of impact factor for scientific development and clinical management. The strength of the literature supports a level one recommendation from the NCCN. This means there is uniform agreement that the treatment should be offered for glioblastoma. The DME medical directors have stated the LCD does not apply to new diagnoses and this treatment has been prescribed throughout the country by hundreds of clinicians to thousands of beneficiaries. Mr. Parks testified, in relevant part, how the Beneficiary has been treated under the standard of care. The tumor was removed in April of 2016 and chemotherapy was performed with radiation and she started Optune in September

2016. She remained stable and her MRIs were without recurrence. She has taken Optune alone without Temozolomide since January 2018 without a recurrence and she has 76% compliance. The MRIs show no progression of the disease and the images are provided roughly every 3 months. (Hearing CD).

The Medicare coverage requirements are met. The Beneficiary was diagnosed with right frontal lobe glioblastoma and received Temozolomide at 150 milligrams 5 times a day repeated every 28 days with Optune. (Exh. 2, p. 26). The attending physician prescribed Optune on August 3, 2016 and she administered the device in the home. (Exh. 2, pp. 8, 9). The device was initially delivered on October 5, 2016 and she received bills for September 5, 2017, October 5, 2017, and November 5, 2017 supporting administration on the dates of service. (Exh. 2, pp. 1, 2, 3, 21). An invoice from Novocure is also included for TTF therapy and transducers. (Exh. 2, p. 4). Administrative law judges are not bound by LCDs, but must provide substantial deference. If an LCD is not followed, the ALJ must explain why in the decision. 42 C.F.R. §405.1062. In this case, the undersigned declines to follow the LCD while also providing substantial deference. As described above, local coverage determination (“LCD”) L34823 finds the TTFT not medically reasonable and necessary. But, DME medical directors have stated the LCD does not apply to new diagnoses. (Hearing CD). Studies from the FDA and new literature from the medical community since the LCD was first issued show the treatment is beneficial to patients such as the Appellant and is medically reasonable and necessary. Examining the process for how contractors make coverage determinations is helpful in establishing medical necessity for the service outside the determination. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on general acceptance by the medical community (standard of practice), as supported by sound medical evidence based on scientific data or research studies published in peer-reviewed medical journals, consensus of expert medical opinion (i.e., recognized authorities in the field: or medical opinion derived from consultations with medical associations or other health care experts. MPIM ch. 13 § 7.1. General acceptance in the medical community is supported by sound evidence based on scientific data or research studies. Optune is approved by the FDA for recurrent glioblastoma multiforme. (Exh. 2, p. 78). The FDA discontinuing the initial study for those not receiving it suggests the treatment was medically necessary for the entire group based on scientific data. (Exh. 3, p. 14). Also, a general acceptance in the medical community is documented by electric field therapy inclusion in the NCCN guidelines for treatment with standard brain radiation therapy. (Exh. 2, pp. 31, 32). Finally, sound medical evidence is shown in the study published by the Journal of the American Medical Association (“JAMA”) finding adding TTFields to maintenance chemotherapy significantly prolonged progress-free and overall survival. Medical opinion derived from consultations with a medical association is shown by the study as well. (Exh. 2, p. 43). The QIC determined the literature does not support the treatment was effective. (Exh. 1, p. 4). But, effectiveness is shown by the included documentation and by the FDA discontinuing the study because it would have been unethical to withhold treatment. The Appellant’s course followed guidelines published by the NCCN and she improved to the point where Optune was provided without Temozolomide. (Hearing CD). The prior studies and the Appellant’s response support the treatment was medically reasonable and necessary for new glioblastoma diagnoses. Therefore, the Medicare coverage requirements are met for the dates of service in this case.

The service is medically reasonable and necessary under Section 1862(a)(1)(A) of the Social Security Act. The Appellant is entitled to Medicare coverage for the Elec Stim Cancer Treatment (E0766) provided on the dates of service.

CONCLUSIONS OF LAW

Accordingly and after careful consideration, there is sufficient evidence supporting the Elec Stim Cancer Treatment (E0766) provided on the dates of service meets Medicare coverage criteria. The service was medically reasonable and necessary as required by Section 1862(a)(1)(A) of the Act and the Appellant is entitled to Medicare coverage.

ORDER

The Medicare Contractor is **DIRECTED** to process the appeal in accordance with this decision.

JAN - 8 2019

SO ORDERED.

Dated: _____

Jeffrey S. Gulin
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Arlington Field Office
Arlington, Virginia

Appellant:	REDACTED	ALJ Appeal No.:	1-8005086977
Beneficiary:		Medicare Part B	
HICN:		Before:	Jeffrey S. Gulin U.S. Administrative Law Judge

DECISION

After considering the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is entered for the Appellant/Beneficiary.

PROCEDURAL HISTORY

REDACTED ("Appellant/Beneficiary") seeks coverage for Elec Stim Cancer Treatment (E0766) provided on September 22, 2017, October 22, 2017, November 22, 2017, and December 22, 2017 ("the Dates of Service"). (Exh. 1, p. 4). The Medicare Administrative Contractor ("MAC"), denied coverage initially and on redetermination. Following the denial, the Appellant requested reconsideration from a Qualified Independent Contractor ("QIC"). On August 13, 2018, the QIC issued an unfavorable reconsideration decision. (Exh. 1, p. 1). The medical documentation received indicates the Beneficiary has a diagnosis of World Health Organization ("WHO") grade IV right frontal glioblastoma. However, the medical documentation does not support the need for the device. There is insufficient documentation to quantify the effects of the device for this beneficiary. No additional medical records have been submitted to explain why this particular beneficiary should be considered for this treatment. In addition, no documentation has been received to show the suggested manufacturer retail price for the service(s) billed. Based on available documentation, payment cannot be allowed. (Exh. 1, p. 5). The QIC determined an Advance Beneficiary Notice ("ABN") was not issued and found Novocure, Inc. ("Supplier") liable for the non-covered amount. (Exh. 1, p. 5).

On September 11, 2018, the Office of Medicare Hearings and Appeals ("OMHA") received the Appellant's request for review by an Administrative Law Judge ("ALJ"). (Exh. 3, p. 1). The amount in controversy meets the statutorily required amount for an ALJ hearing. Judge Jeffrey S. Gulin held a telephone conference hearing on November 29, 2018. Attorney Bridget Noonan provided argument for the Appellant. There were no objections and all exhibits were admitted into the record. (Hearing CD).

ISSUES

1. Whether the Elec Stim Cancer Treatment (E0766) provided to the Beneficiary on the dates of service meet Medicare coverage criteria.
2. Whether the services provided are medically necessary under Section 1862(a)(1)(A) of the Social Security Act ("Act") and covered under Medicare.
3. If the services are found to be excluded from coverage under Section 1862(a)(1)(A), then another issue to be determined is whether payment may nevertheless be made to appellant under the limitation on liability provisions of Section 1879 of the Act.

FINDINGS OF FACT

1. The Beneficiary/Appellant is seeking Medicare coverage for Elec Stim Cancer Treatment (E0766) provided on the dates of service. (Exh. 1, p. 4). A letter from the Centers for Medicare and Medicaid Services ("CMS") indicates NovoTTF-110A Systems fall in the definition for durable medical equipment ("DME"). (Exh. 2, p. 82).
2. The attending physician originally prescribed TTF therapy on December 14, 2015. (Exh. 2, p. 3). An Optune device was first delivered to the Beneficiary/Appellant on February 22, 2016. (Exh. 2, p. 18).
3. Treatment encounter notes show the Beneficiary was diagnosed with right frontal glioblastoma grade IV and underwent a resection at the University of Tennessee and pathology was consistent with the glioblastoma. Temodar was recommended with the Optune device and further administration was directed on May 17, 2017. (Exh. 2, p. 23).
4. The attending physician prescribed Optune to the Beneficiary on October 10, 2017 for glioblastoma and she was to use the treatment within a 6-month period. (Exh. 2, p. 1). A narrative from the attending physician describes how the treatment was approved by the FDA in October 2015 for use in combination with Temozolomide for adult patients with new diagnoses, supratentorial glioblastoma following maximal de-bulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy. (Exh. 2, p. 4). Assessment of need from the manufacturer, Novocure, Inc., shows Optune would be administered in the home. (Exh. 2, p. 6).
5. An article included from NovoCure with the product dossier describes Food and Drug Administration ("FDA") approval for treatment of recurrent glioblastoma Multiforme. The FDA gave premarket approval ("PMA") for the device in 2011. (Exh. 2, p. 94).
6. Included in the record is a study entitled "NovoTTF-100A versus physician's choice chemotherapy in recurrent glioblastoma: A randomized phase III trial of a novel treatment modality" published in SciVerse Science Direct. (Exh. 2, p. 138). Participants in the study were randomized at a 1 to 1 ratio to receive either TTF monotherapy or the best available chemotherapy according to the local physician's choice. (Exh. 2, p. 140). The trial compared standard chemotherapy per local practice with TTF in a prospective, multi-centered phase III trial. Although the trial did not reach its primary end-point of improved

survival compared to active chemotherapy, this new minimally invasive and chemotherapy-free local treatment modality demonstrated a statistically non-significant increased response rate (14 versus 9.6%, $P = 0.19$), an improved PFS6 rate (21% versus 15%, $p = 0.13$), and a trend toward reduction of the risk of death (hazard ratio 0.86, 95% CI 0.66-1.12, $p = 0.27$); as well as sustained improvement in QOL. (Exh. 2, p. 145). Based on the results of this study, TTF therapy has recently been approved in the US and Europe for the treatment of recurrent glioblastoma. (Exh. 2, p. 146).

7. Another article found “TTFields alone and in combination with chemotherapeutic agents effectively reduce the viability of MDR cell sub-lines that over-express ABC transporters.” Conclusions from the study found TTFields alone in combination with paclitaxel and doxorubicin effectively reduce viability of both wild type and MDR cell sub-lines and thus can potentially be used as an effective treatment of drug resistant tumors. (Exh. 2, p. 174). Results in a study entitled “Chemotherapeutic treatment efficacy and sensitivity are increased by adjuvant alternating electric fields (TTFields)” found combining chemotherapeutic cancer treatment with TTFields may increase chemotherapeutic efficacy and sensitivity without increasing treatment related toxicity. The article was published by BioMed Central. (Exh. 2, p. 181). BioMed Central describes itself as “an evolving portfolio of some 300 peer-reviewed journals, sharing discoveries from research communities in science, technology, engineering and medicine.” (BioMed Central (“BMC”), About, at <https://www.biomedcentral.com/about>).
8. A study published in the 2015 Journal of the American Medical Association (“JAMA”) edition entitled “Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma – A Randomized Clinical Trial” found in the interim analysis of 315 patients with glioblastoma who completed standard chemo radiation therapy, adding TTFields to maintenance temozolomide chemotherapy significantly prolonged progress-free and overall survival. (Exh. 2, p. 46).
9. Electric field therapy is included in the National Comprehensive Care Network (“NCCN”) guidelines for treatment with standard brain radiation therapy for central nervous system cancers for 2016. (Exh. 2, pp. 42, 43). The FDA deemed it unethical to withhold TTFT from those not receiving it during the clinical trial and ordered the sponsor to discontinue the study. (Hearing CD).

LEGAL FRAMEWORK

A. Jurisdiction/Scope of Review/Standard of Review

OMHA has jurisdiction to hear appeals of QIC reconsiderations. 42 C.F.R. § 405.1002. ALJ decisions bind parties unless the Medicare Appeals Council (“Council”) reviews or the case is escalated to Federal district court. 42 C.F.R. § 405.1048. ALJ decisions are reviewed by the Council in accordance with §§ 405.980, 405.1110, and 405.1138.

The issues before the ALJ include issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the appellant’s favor. 42 C.F.R. § 405.1032(a). The ALJ conducts *de novo* review and issues a decision based on the record. 42 C.F.R. § 405.1000(d).

PRINCIPLES OF LAW

A. Statutes and Regulations

Section 1831 establishes the Supplemental Medical Insurance Program for the aged and disabled under Medicare Part B. Section 1832 establishes the scope of benefits that are provided to beneficiaries under the Medicare Part B insurance program. Under § 1832(a)(2)(B), an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with them made by a provider of services. (*See also* 42 CFR § 410.3). Section 1833(e) provides that “[n]o payment shall be made to any provider of services . . . unless there has been furnished such information as may be necessary in order to determine the amounts due such provider” (*See also* 42 CFR § 424.5(a)(6)).

Section 1862(a)(1)(A) of Title XVIII of the Social Security Act (SSA) excludes expenses incurred for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Section 1861(s)(6) defines the term “medical and other health services.” (*See also* 42 CFR § 410.10(h)). Also considered is 42 CFR § 414.200-232 implementing §§ 1834 (a) and (h) of the Act by specifying how payments are made for the purchase or rental of new and used durable medical equipment and prosthetic and orthotic devices for Medicare beneficiaries. Section 1862(a)(1)(A) provides that notwithstanding any other provision of the Act, no payment shall be made for any expenses incurred for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. (*See also* 42 CFR § 411.15(k)).

The Centers for Medicare & Medicaid Services (CMS), the federal agency that administers the Medicare program, has established a coding system for screening, processing, identifying, and paying Medicare claims—the Healthcare Common Procedure Coding System (HCPCS). The HCPCS incorporates codes developed by the American Medical Association, Current Procedure Terminology (CPT) codes, to identify and describe medical services and items. (*See* 42 C.F.R. §§ 414.2, 414.40).

B. National Coverage Determinations

A National Coverage Determination (“NCD”), if applicable, is binding on the ALJ. 42 C.F.R. §405.1060(a)(4).

C. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by Centers for Medicare and Medicaid Services (“CMS”), no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. §405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that establishes criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (“LCDs”).

Administrative Law Judges are not bound by LCDs, but will give substantial deference to these policies when applicable. If an Administrative Law Judge does not follow a policy in a particular case, the Administrative Law Judge must explain why in the decision. 42 C.F.R. §405.1062.

When a NCD or LCD or other directives are lacking, the adjudication process requires the Judge to determine coverage by performing the same review that Medicare contractors, according to the Medicare Program Integrity Manual (Publ. 100-08), Chapter 13.7.1, would perform when developing a LCD.

Contractor LCDs shall be based on the strongest evidence available. The extent and quality of supporting evidence is key to defending challenges to LCDs. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on:

- Published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and
- General acceptance by the medical community (standard of practice), as supported by sound medical evidence based on:
- Scientific data or research studies published in peer-reviewed medical journals;
- Consensus of expert medical opinion (i.e., recognized authorities in the field: or
- Medical opinion derived from consultations with medical associations or other health care experts.

Local Coverage Determination L34823 entitled “Tumor Treatment Field Therapy” provides coverage guidance in this case: Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. Policy Article A52711 provides further guidance by stating “in order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met.”

ANALYSIS

The QIC issued an unfavorable reconsideration decision. (Exh. 1, p. 1). The medical documentation received indicates the Beneficiary has a diagnosis of WHO grade IV right frontal glioblastoma. The medical documentation does not support the need for the device. There is insufficient documentation to quantify the effects of the device for this beneficiary. No additional medical records have been submitted to explain why this particular beneficiary should be considered for this treatment. In addition, no documentation has been received to show the suggested manufacturer retail price for the service(s) billed. Based on available documentation, payment cannot be allowed. (Exh. 1, p. 5).

Local Coverage Determination L34823 entitled “Tumor Treatment Field Therapy” provides coverage guidance in this case: Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. National Government Services, Inc. Local Coverage Determination L34823: Tumor Treatment Field Therapy (“TTFT”) (L34823) (October 2017). Policy Article A52711 provides further guidance by stating “in order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met.” Also, administrative law judges are not bound by LCDs, but will give substantial deference to these policies when applicable. If an administrative law judge does not follow a policy in a particular case, the administrative law judge must explain why in the decision. 42 C.F.R. §405.1062.

Attorney Noonan argued the treatment is used to treat rare glioblastoma and the condition is classified as an orphan disease. These orphan diseases do not receive as much funding because they are so rare. Optune broke through a 10-year dry period with nothing new to help the patients. The QIC denied coverage based on insufficient evidence to quantify helping the patients and LCD L34823 was referenced. The DME MAC medical directors also said the LCDs do not apply to new cases of glioblastoma. The Appellant was diagnosed in October 2015 and had surgical resection and she was prescribed Optune in February of 2016. The NCCN recommends coverage and the FDA stopped the clinical trial because the evidence was so compelling, they allowed patients to cross over to the arm where they were getting Optune. It was unethical to withhold treatment. Also, virtually every payer is covering the treatment and it is used in over 800 cancer treatment centers. The Appellant has remained progression free following the start of Optune. This counters the QIC’s statements about the effects of the device not being quantifiable. (Hearing CD).

The Medicare coverage requirements are met in this case. The attending physician originally prescribed TTF therapy on December 14, 2015. (Exh. 2, p. 3). An Optune device was first delivered to the Beneficiary/Appellant on February 22, 2016. (Exh. 2, p. 18). Further treatment encounter notes describe how the Beneficiary was diagnosed with right frontal glioblastoma grade IV and she underwent a resection at the University of Tennessee and pathology was consistent with the glioblastoma. Temodar was recommended with the Optune device and continued Optune administration was directed on May 17, 2017. This treatment continued on into the dates of service (Exh. 2, p. 23). Administrative law judges are not bound by LCDs, but must provide substantial deference. If an LCD is not followed, the ALJ must explain why in the decision. 42 C.F.R. § 405.1062. In this case, the undersigned declines to follow the LCD while also providing substantial deference. As described above, local coverage determination (“LCD”) L34823 finds the TTFT not medically reasonable and necessary. But, studies from the FDA and new literature from the medical community since the LCD was first issued show the treatment is beneficial to patients such as the Appellant and is medically reasonable and necessary. Examining the process for how contractors make coverage decisions is helpful in establishing medical necessity for the service outside the determination. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on general acceptance by the medical community (standard of practice), as supported by sound medical evidence based on scientific data or research studies published in peer-reviewed medical journals, consensus of expert medical opinion (i.e., recognized authorities in the field; or medical opinion derived from consultations with medical associations or other

health care experts. MPIM ch. 13 § 7.1. General acceptance in the medical community is supported by sound evidence based on scientific data or research studies. Optune is approved by the FDA for recurrent glioblastoma Mutiforme. (Exh. 2, p. 94). Also, the FDA discontinuing the initial study for those not receiving treatment suggests it was necessary for the entire group based on scientific data. (Hearing CD). Further general acceptance in the medical community is documented by electric field therapy inclusion in the NCCN guidelines for treatment with standard brain radiation therapy. (Exh. 2, pp. 42, 43). Several other studies in the record also support coverage. Sound medical evidence is shown in the study published by the Journal of the American Medical Association ("JAMA") finding TTFields with maintenance chemotherapy significantly prolonged progress-free and overall survival. Medical opinion derived from consultations with a medical association is also shown by the study. (Exh. 2, p. 46). Finally, the article entitled "Chemotherapeutic treatment efficacy and sensity are increased by adjuvant alternating electric fields (TTFields)" found combining chemotherapeutic cancer treatment with TTFields may increase chemotherapeutic efficacy and sensitivity without increasing treatment related toxicity. (Exh. 2; p. 181). This article is also peer reviewed to support coverage under MPIM criteria described above. (BioMed Central ("BMC"), About, at <https://www.biomedcentral.com/about>). The QIC determined the record does not support need for the device. (Exh. 1, p. 5). The effectiveness and need is shown, however, by FDA discontinuing the study as described, the Appellant's treatment following guidelines published by the NCCN, the further studies included in the record, and also the halt in progression as described during the hearing. (Hearing CD). The Medicare coverage requirements are therefore met for the Optune treatment on the dates of service in this case.

The service is medically reasonable and necessary under Section 1862(a)(1)(A) of the Social Security Act. The Appellant is entitled to Medicare coverage for the Elec Stim Cancer Treatment (E0766) provided on the dates of service.

CONCLUSIONS OF LAW

Accordingly and after careful consideration, there is sufficient evidence supporting the Elec Stim Cancer Treatment (E0766) provided on the dates of service meets Medicare coverage criteria. The service was medically reasonable and necessary as required by Section 1862(a)(1)(A) of the Act and the Appellant is entitled to Medicare coverage.

ORDER

The Medicare Contractor is **DIRECTED** to process the appeal in accordance with this decision.

DEC 06 2018

SO ORDERED.

Dated: _____

Jeffrey S. Gulin
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of: **NOVOCURE INC.**

OMHA Appeal No.: **1-2489188369**

Beneficiary:

Medicare: **Part B**

HICN: *******0528A**

Before: **Hon. Roberto M. Gutierrez**
U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, , received miscellaneous durable medical equipment ("DME"), NovoTTF-100A System (E1399) from the Appellant on July 9, 2013, and miscellaneous DME accessory (A9900) on June 7, 2013 and July 23, 2013, the dates of service at issue. The Appellant's claim to Medicare was denied by CGS Administrators, LLC, a Medicare Administrative Contractor ("Contractor"), upon initial and redetermination. On January 17, 2014, C2C Solutions, Inc., a Medicare Qualified Independent Contractor ("QIC"), upheld the prior denials upon reconsideration review. By correspondence received on February 12, 2014, the Appellant made a timely request for an Administrative Law Judge ("ALJ") hearing before the Office of Medicare Hearings and Appeals ("OMHA"). 42 C.F.R. § 405.1014(b)(1).

On July 27, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference. The Appellant's additional evidence was excluded from the record as good cause was not found to admit the new evidence because the evidence was duplicative.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399), and miscellaneous DME accessory (A9900) provided to the Beneficiary on the dates of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on January 17, 2014 (*Id.*). By correspondence received on February 12, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: "There is insufficient documentation to quantify the effects of the device for this beneficiary. No additional medical records have been submitted to explain why this particular beneficiary should be considered for this treatment. In addition, no documentation has been received to show the suggested manufacturer retail price for the service(s) billed" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on July 9, 2013, and a NovoTTF-100A System transducer arrays billed under miscellaneous DME accessory (A9900) on June 7, 2013 and July 23, 2013.

The Beneficiary has a medical history that includes recurrent glioblastoma multiforme ("GBM") (Ex. 2). He underwent a stereotactic right occipital with volumetric resection and then began chemotherapy and radiation treatment (*Id.*). Despite this treatment, he had both clinical and radiographic progression of disease (*Id.*). On May 22, 2013, his treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy ("TTFT") (*Id.*). The clinical records indicate that after initiating TTFT, the Beneficiary's condition stabilized (*Id.*).

The Food and Drug Administration ("FDA") approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population (Ex. 1). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009 (Ex. 2). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life (*Id.*).

The record includes a publication from the National Comprehensive Cancer Network ("NCCN") Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," which reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM (*Id.*). Along with

palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment (*Id.*).

At the hearing, the Appellant's representative testified that Optune (which was previously known as the NovoTTF-100A system) is a portable, wearable device that delivers tumor treating fields, which are alternating electric fields, to the brain. The device consists of a portable, electric field generator connected to a portable battery that is connected to 4 insulated transducer arrays that are placed on the patient's scalp. The device generates electric currents that go through the transducer arrays, which creates the tumor treating fields. In 2013, after receiving billing rights from CMS, the Appellant billed the device under 2 components: (1) the electric field generator, billed under E1399; and (2) the insulated transducer arrays, billed as a DME supply under miscellaneous code A9900. In 2014, effective January 1, 2014, CMS issued two HCPCS codes for the NovoTTF-100A system: E0766 for the device; and A4555 for the transducer arrays. At that time, CMS designated the therapy as DME requiring frequent and substantial servicing.

The therapy delivers alternating electric fields to the brain. The electric fields disrupt the formation of the mitotic spindle in the dividing cancer cell. The therapy is similar to taxing chemotherapy insofar as it inhibits the formation of the mitotic spindle, which leads to program cell death. The therapy does not affect non-dividing cells and is frequency-tuned specifically to GBM cells.

The therapy was approved by the FDA in 2011 under the pre-market approval pathway, which is the most stringent device approval pathway. Only 2% of medical devices are approved through this pathway. That approval was based on a randomized controlled trial in recurrent GBM of 243 patients that compared using Optune by itself to physician-choice chemotherapy. The FDA concluded in its initial approval that the NovoTTF-100A system treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness, and a better quality of life compared to chemotherapy in the control arm of the study. This trial was published in the *European Journal of Cancer* in 2012, which is a CMS-recognized medical journal. According to the Appellant, Optune is included in the NCCN Guidelines with a consensus 2B recommendation for recurrent GBM and a 2A uniform consensus recommendation for newly diagnosed GBM in combination with temozolomide.

The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary. The therapy was established and proven as an option for recurrent GBM through peer reviewed journals, clinical guidelines and is widely recognized in the field nationwide. GBM is an aggressive, primary brain cancer. Prior to Optune being FDA approved, patients had a life expectancy with treatment of about 12 to 15 months. A disease is labeled recurrent after a patient has progressed after initial therapy. A 1 year survival rate for a recurrent GBM patient is about 10%. When GBM recurs, about 20% of patients are eligible for a reoperation or an additional resection. Most patients are not eligible for additional radiation because they have already maxed out their radiation dose with the initial treatment. A chemotherapy regimen that has already been tried and failed is not an option when a tumor recurs or progresses post-treatment. As a result, recurrent GBM patients have very limited treatment options.

The Appellant's representative further testified that the Beneficiary was diagnosed with a right hemisphere GBM in September 2012. He received surgical resection with pathology confirming GBM. He completed standard chemoradiation with temozolomide. He developed a recurrence and was started on Avastin. He developed further recurrence and Avastin and temozolomide were discontinued. His treating physician recommended Optune, which he began on January 9, 2013. In the medical records submitted, he had a subsequent CAT scan evaluation of his tumor dated May 22, 2013 (which was several months after he was started on Optune) that showed stable disease. He remained on therapy for an additional 4 months. He had recurrent GBM and was on his third progression at the time of therapy. There were no other FDA-approved options for his recurrent GBM. At the time he utilized the therapy, Optune was FDA-approved for his specific condition. In addition, the NCCN Guidelines recommend Optune for this indication, with a category 2B level of evidence and consensus.

The Appellant's representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The Appellant's representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

Principles of Law

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges ("ALJ's") within OMHA issue binding decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.*

For requests filed in calendar years 2010 through 2012, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible) and \$140.00 for calendar years 2013 through 2014. *See* §1869(b)(1)(E) of the Act, 74 Fed. Reg. 48976 (Sept. 2, 2009), 75 Fed. Reg. 58407 (Sept. 23, 2010), 76 Fed. Reg. 59138 (Sept. 23, 2011), 77 Fed. Reg. 59619 (Sept. 28, 2012), 78 Fed. Reg. 59702 (Sept. 27, 2013), 42 C.F.R. § 405.1006(b), and 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. Section 557 of the Administrative Procedure Act and 70 Fed. Reg. 36386 (June 23, 2005). *De novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into in the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. *See* 42 C.F.R. § 405.1018. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. *See* 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Social Security Act

Medicare Part B provides coverage to eligible beneficiaries for all or part of the cost of "medical and other health services," a term which is defined by the Act as including, among many other

things, durable medical equipment.” *Sections 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Social Security Act; 42 C.F.R. §410.10(h).*

No Medicare payment can be allowed for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member *Section 1862(a)(1)(A) of Title XVIII of the Social Security Act; 42 C.F.R. §411.15(k)(2).*

No payment can be made to the provider or another person unless such information, as may be necessary, has been furnished in support of the medical necessity of the claimed services in order to determine the amount due such provider or other individual. *Section 1833 of Title XVIII of the Social Security Act; 42 C.F.R. §424.5(a)(6).*

When Medicare coverage is precluded under Section 1862(a)(1)(A), i.e., the item was not reasonable and necessary, payment will be made, notwithstanding the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably be expected to know that the item was not covered. This provision is commonly referred to as the limitation of liability provision. *Section 1879 of Title XVIII of the Social Security Act, 42 C.F.R. §411.400.*

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than National Coverage Determinations, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also 42 C.F.R. §405.860.* However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals or local coverage determinations (“LCDs”). 42 C.F.R. § 405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs) or Center for Medicare Services (“CMS”) program guidance when applicable. There is no applicable LCD in the instant case.

Analysis

The amount in controversy is in excess of \$140.00. The QIC issued an unfavorable reconsideration decision on January 17, 2014. By correspondence received on February 12, 2014, the Appellant made a request for an ALJ hearing before OMHA. Therefore, the Appellant’s request was made in a timely manner and the claim satisfies the jurisdictional requirements for an ALJ Hearing before OMHA.

The QIC in its unfavorable decision stated, in part, as follows: “There is insufficient documentation to quantify the effects of the device for this beneficiary. No additional medical records have been submitted to explain why this particular beneficiary should be considered for this treatment. In addition, no documentation has been received to show the suggested manufacturer retail price for the service(s) billed” (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on July 9, 2013, and a NovoTTF-100A System transducer arrays billed under miscellaneous DME accessory (A9900) on June 7, 2013 and July 23, 2013.

The Beneficiary has a medical history that includes recurrent GBM (Ex. 2). He underwent a stereotactic right occipital with volumetric resection and then began chemotherapy and radiation treatment (*Id.*). Despite this treatment, he had both clinical and radiographic progression of disease (*Id.*). On May 22, 2013, his treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*). The clinical records indicate that after initiating TTFT, the Beneficiary's condition stabilized (*Id.*).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category (*See Ex 2*). Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "*as a factor* in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment. In addition, the record indicates that after the Beneficiary initiated TTFT with the NovoTTF-100A system, his condition was deemed stable in June 2013.

The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had recurrent GBM and was on his third progression at the time of therapy. There were no other FDA-approved options for his recurrent GBM. In the medical records submitted, he had a subsequent CAT scan evaluation of his tumor dated May 22, 2013 (which was several months after he was started on Optune) that showed stable disease. He remained on therapy for an additional 4 months. At the time he utilized the therapy, Optune was FDA-approved for his specific condition. In addition, the NCCN Guidelines recommend Optune for this indication, with a category 2B level of evidence and consensus.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTFT has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. Since the NovoTTF-100A System at issue is medically reasonable and necessary, the NovoTTF-100A System transducer arrays is also covered under Section 1862(a)(7) of the Social Security Act. As such, Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399), and miscellaneous DME accessory (A9900) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Conclusions of Law

Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399), and miscellaneous DME accessory (A9900) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

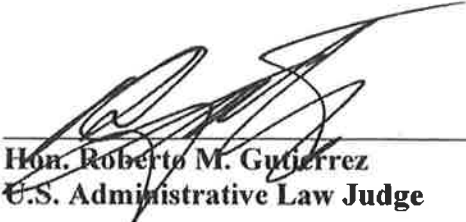
Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

AUG 23 2017

Dated:


Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



1525

**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida**

Appeal of: NOVOCURE INC.	OMHA Appeal No.: 1-2454863966
Beneficiary:	Medicare: Part B
HICN: *****2452A	Before: Hon. Roberto M. Gutierrez U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, , received miscellaneous durable medical equipment ("DME"), NovoTTF-100A System (E1399) from the Appellant on April 2, 2013, May 2, 2013 and June 2, 2013, the dates of service at issue. The Appellant's claim to Medicare was denied by NHIC, a Medicare Administrative Contractor ("Contractor"), upon initial and redetermination. On December 5, 2013, C2C Solutions, Inc., a Medicare Qualified Independent Contractor ("QIC"), upheld the prior denials upon reconsideration review. By correspondence received on January 23, 2014, the Appellant made a timely request for an Administrative Law Judge ("ALJ") hearing before the Office of Medicare Hearings and Appeals ("OMHA"). 42 C.F.R. § 405.1014(b)(1).

On July 27, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. The Appellant submitted evidence to the undersigned not previously submitted to the QIC or a prior decision maker, which the undersigned found "good cause" for admitting into the record as Exhibit 5, as such evidence is necessary for the full development of the administrative record. 42 C.F.R. §§ 405.1018 and 405.1028. However, some of the Appellant's additional evidence was excluded from the record as good cause was not found to admit this new evidence because the evidence was duplicative. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the dates of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on December 5, 2013 (*Id.*). By correspondence received on January 23, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: "The item provided to the beneficiary is not covered under Medicare regulations and as such, payment cannot be effected for the NOVOTTF-100A System at issue" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on April 2, 2013, May 2, 2013 and June 2, 2013.

The 66 year-old Beneficiary has a medical history that includes recurrent glioblastoma multiforme ("GBM") (Ex. 2). She underwent a subtotal resection and then began chemotherapy and radiation treatment (*Id.*). On February 22, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy ("TTFT") (Ex. 5).

The Food and Drug Administration ("FDA") approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (Ex. 2). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population (*Id.*). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009 (*Id.*). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life (*Id.*).

The record includes a publication from the National Comprehensive Cancer Network ("NCCN") Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," which reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM (*Id.*). Along with

palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment (*Id.*).

At the hearing, the Appellant's representative testified that Optune (which was previously known as the NovoTTF-100A system) is a portable, wearable device that delivers tumor treating fields, which are alternating electric fields, to the brain. The device consists of a portable, electric field generator connected to a portable battery that is connected to 4 insulated transducer arrays that are placed on the patient's scalp. The device generates electric currents that go through the transducer arrays, which creates the tumor treating fields. In 2013, after receiving billing rights from CMS, the Appellant billed the device under 2 components: (1) the electric field generator, billed under E1399; and (2) the insulated transducer arrays, billed as a DME supply under miscellaneous code A9900. In 2014, effective January 1, 2014, CMS issued two HCPCS codes for the NovoTTF-100A system: E0766 for the device; and A4555 for the transducer arrays. At that time, CMS designated the therapy as DME requiring frequent and substantial servicing.

The therapy delivers alternating electric fields to the brain. The electric fields disrupt the formation of the mitotic spindle in the dividing cancer cell. The therapy is similar to taxing chemotherapy insofar as it inhibits the formation of the mitotic spindle, which leads to program cell death. The therapy does not affect non-dividing cells and is frequency-tuned specifically to GBM cells.

The therapy was approved by the FDA in 2011 under the pre-market approval pathway, which is the most stringent device approval pathway. Only 2% of medical devices are approved through this pathway. That approval was based on a randomized controlled trial in recurrent GBM of 243 patients that compared using Optune by itself to physician-choice chemotherapy. The FDA concluded in its initial approval that the NovoTTF-100A system treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness, and a better quality of life compared to chemotherapy in the control arm of the study. This trial was published in the *European Journal of Cancer* in 2012, which is a CMS-recognized medical journal. According to the Appellant, Optune is included in the NCCN Guidelines with a consensus 2B recommendation for recurrent GBM and a 2A uniform consensus recommendation for newly diagnosed GBM in combination with temozolomide.

The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary. The therapy was established and proven as an option for recurrent GBM through peer reviewed journals, clinical guidelines and is widely recognized in the field nationwide. GBM is an aggressive, primary brain cancer. Prior to Optune being FDA approved, patients had a life expectancy with treatment of about 12 to 15 months. A disease is labeled recurrent after a patient has progressed after initial therapy. A 1 year survival rate for a recurrent GBM patient is about 10%. When GBM recurs, about 20% of patients are eligible for a reoperation or an additional resection. Most patients are not eligible for additional radiation because they have already maxed out their radiation dose with the initial treatment. A chemotherapy regimen that has already been tried and failed is not an option when a tumor recurs or progresses post-treatment. As a result, recurrent GBM patients have very limited treatment options.

The Appellant's representative further testified that the Beneficiary was diagnosed with a right frontal GBM in September 2012, and received a subtotal surgical resection with histologically confirmed GBM. She completed standard field cranial irradiation in September and October 2012. She was admitted for drug induced jaundice and rash in December 2012, related to her drug induced hepatitis diagnosis. She began Optune on February 22, 2013. She utilized the device at least 18 hours a day per the FDA label and the treatment was well tolerated according to the medical record. During treatment, she saw an improvement in her physical and motor function and participated in physical therapy. She had recurrent GBM and was on her second progression at the time of her therapy. There were no other FDA approved treatment options available to her for her recurrent GBM. Her physician prescribed Optune as the only FDA approved option left for her to try. At the time of therapy, Optune was FDA-approved for her specific condition, and the standard of care treatment guidelines recommended Optune for this indication, with a category 2B level of evidence and consensus.

The Appellant's representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The Appellant's representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

Principles of Law

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges

("ALJ's") within OMHA issue binding decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.*

For requests filed in calendar years 2010 through 2012, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible) and \$140.00 for calendar years 2013 through 2014. *See* §1869(b)(1)(E) of the Act, 74 Fed. Reg. 48976 (Sept. 2, 2009), 75 Fed. Reg. 58407 (Sept. 23, 2010), 76 Fed. Reg. 59138 (Sept. 23, 2011), 77 Fed. Reg. 59619 (Sept. 28, 2012), 78 Fed. Reg. 59702 (Sep. 27, 2013), 42 C.F.R. § 405.1006(b), and 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. Section 557 of the Administrative Procedure Act and 70 Fed. Reg. 36386 (June 23, 2005). *De novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into in the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. *See* 42 C.F.R. § 405.1018. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. *See* 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Social Security Act

Medicare Part B provides coverage to eligible beneficiaries for all or part of the cost of “medical and other health services,” a term which is defined by the Act as including, among many other things, durable medical equipment.” *Sections 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Social Security Act; 42 C.F.R. §410.10(h).*

No Medicare payment can be allowed for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member *Section 1862(a)(1)(A) of Title XVIII of the Social Security Act; 42 C.F.R. §411.15(k)(2).*

No payment can be made to the provider or another person unless such information, as may be necessary, has been furnished in support of the medical necessity of the claimed services in order to determine the amount due such provider or other individual. *Section 1833 of Title XVIII of the Social Security Act; 42 C.F.R. §424.5(a)(6).*

When Medicare coverage is precluded under Section 1862(a)(1)(A), i.e., the item was not reasonable and necessary, payment will be made, notwithstanding the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably be expected to know that the item was not covered. This provision is commonly referred to as the limitation of liability provision. *Section 1879 of Title XVIII of the Social Security Act, 42 C.F.R. §411.400.*

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than National Coverage Determinations, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also 42 C.F.R. §405.860.* However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals or local coverage determinations (“LCDs”). 42 C.F.R. § 405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs) or Center for Medicare Services (“CMS”) program guidance when applicable. There is no applicable LCD in the instant case.

Analysis

The amount in controversy is in excess of \$140.00. The QIC issued an unfavorable reconsideration decision on December 5, 2013. By correspondence received on January 23, 2014, the Appellant made a request for an ALJ hearing before OMHA. Therefore, the Appellant’s request was made in a timely manner and the claim satisfies the jurisdictional requirements for an ALJ Hearing before OMHA.

The QIC in its unfavorable decision stated, in part, as follows: "The item provided to the beneficiary is not covered under Medicare regulations and as such, payment cannot be effected for the NOVOTTF-100A System at issue" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on April 2, 2013, May 2, 2013 and June 2, 2013.

The 66 year-old Beneficiary has a medical history that includes recurrent GBM (Ex. 2). She underwent a subtotal resection and then began chemotherapy and radiation treatment (*Id.*). On February 22, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (Ex. 5).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (Ex. 2). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category (*See* Ex 2). Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "*as a factor* in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment.

The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had recurrent GBM and was on her second progression at the time of therapy. Following standard field cranial irradiation in September and October 2012, she was admitted for drug induced jaundice and rash in December 2012, related to her drug induced hepatitis diagnosis. There were no other FDA approved treatment options for her at the time her physician prescribed Optune. She utilized the device at least 18 hours a day per the FDA label and the treatment was well tolerated according to the medical record. During treatment, she saw an improvement in her physical and motor function and participated in physical therapy. At the time of therapy, Optune was FDA-approved for her specific condition, and the standard of care treatment guidelines recommended Optune for this indication, with a category 2B level of evidence and consensus.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTFT has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. As such, Medicare coverage

exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Conclusions of Law


Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated:



Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge

AUG 25 2017



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of: **NOVOCURE INC.**

OMHA Appeal No.: **1-2518729667**

Beneficiary:

Medicare: **Part B**

HICN: *******0839A**

Before: **Hon. Roberto M. Gutierrez**
U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, received miscellaneous durable medical equipment ("DME"), NovoTTF-100A System (E1399) from the Appellant on April 3, 2013, May 3, 2013, June 3, 2013 and July 3, 2013, and miscellaneous DME accessory (A9900) on April 3, 2013 and May 1, 2013, the dates of service at issue. The Appellant's claim to Medicare was denied by CGS Administrators, LLC, a Medicare Administrative Contractor ("Contractor"), upon initial and redetermination. On January 16, 2014, C2C Solutions, Inc., a Medicare Qualified Independent Contractor ("QIC"), upheld the prior denials upon reconsideration review. By correspondence received on February 28, 2014, the Appellant made a timely request for an Administrative Law Judge ("ALJ") hearing before the Office of Medicare Hearings and Appeals ("OMHA"). 42 C.F.R. § 405.1014(b)(1).

On July 27, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference. The Appellant's additional evidence was excluded from the record as good cause was not found to admit the new evidence because the evidence was duplicative.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399), and miscellaneous DME accessory (A9900) provided to the Beneficiary on the dates of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on January 16, 2014 (*Id.*). By correspondence received on February 28, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: "There is insufficient documentation to quantify the effects of the device for this beneficiary. No additional medical records have been submitted to explain why this particular beneficiary should be considered for this treatment. In addition, no documentation has been received to show the suggested manufacturer retail price for the service(s) billed. Based on the available documentation, payment cannot be allowed" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on April 3, 2013, May 3, 2013, June 3, 2013 and July 3, 2013, and INE Insulated Transducer Arrays billed under miscellaneous DME accessory (A9900) on April 3, 2013 and May 1, 2013.

The Beneficiary has a medical history that includes right parietal glioblastoma multiforme ("GBM") (Ex. 2). He underwent a total resection and then began chemotherapy and radiation treatment (*Id.*). His treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy ("TTFT") (*Id.*).

The Food and Drug Administration ("FDA") approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population (*Id.*). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009 (*Id.*). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life (*Id.*).

The record includes a publication from the National Comprehensive Cancer Network ("NCCN") Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," which reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM (*Id.*). Along with

palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment (*Id.*).

At the hearing, the Appellant's representative testified that Optune (which was previously known as the NovoTTF-100A system) is a portable, wearable device that delivers tumor treating fields, which are alternating electric fields, to the brain. The device consists of a portable, electric field generator connected to a portable battery that is connected to 4 insulated transducer arrays that are placed on the patient's scalp. The device generates electric currents that go through the transducer arrays, which creates the tumor treating fields. In 2013, after receiving billing rights from CMS, the Appellant billed the device under 2 components: (1) the electric field generator, billed under E1399; and (2) the insulated transducer arrays, billed as a DME supply under miscellaneous code A9900. In 2014, effective January 1, 2014, CMS issued two HCPCS codes for the NovoTTF-100A system: E0766 for the device; and A4555 for the transducer arrays. At that time, CMS designated the therapy as DME requiring frequent and substantial servicing.

The therapy delivers alternating electric fields to the brain. The electric fields disrupt the formation of the mitotic spindle in the dividing cancer cell. The therapy is similar to taxing chemotherapy insofar as it inhibits the formation of the mitotic spindle, which leads to program cell death. The therapy does not affect non-dividing cells and is frequency-tuned specifically to GBM cells.

The therapy was approved by the FDA in 2011 under the pre-market approval pathway, which is the most stringent device approval pathway. Only 2% of medical devices are approved through this pathway. That approval was based on a randomized controlled trial in recurrent GBM of 243 patients that compared using Optune by itself to physician-choice chemotherapy. The FDA concluded in its initial approval that the NovoTTF-100A system treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness, and a better quality of life compared to chemotherapy in the control arm of the study. This trial was published in the *European Journal of Cancer* in 2012, which is a CMS-recognized medical journal. According to the Appellant, Optune is included in the NCCN Guidelines with a consensus 2B recommendation for recurrent GBM and a 2A uniform consensus recommendation for newly diagnosed GBM in combination with temozolomide.

The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary. The therapy was established and proven as an option for recurrent GBM through peer reviewed journals, clinical guidelines and is widely recognized in the field nationwide. GBM is an aggressive, primary brain cancer. Prior to Optune being FDA approved, patients had a life expectancy with treatment of about 12 to 15 months. A disease is labeled recurrent after a patient has progressed after initial therapy. A 1 year survival rate for a recurrent GBM patient is about 10%. When GBM recurs, about 20% of patients are eligible for a reoperation or an additional resection. Most patients are not eligible for additional radiation because they have already maxed out their radiation dose with the initial treatment. A chemotherapy regimen that has already been tried and failed is not an option when a tumor recurs or progresses post-treatment. As a result, recurrent GBM patients have very limited treatment options.

The Appellant's representative further testified that the Beneficiary was diagnosed with a right parietal GBM in May 2011. He underwent a gross total surgical resection in the same month, with pathology confirming GBM. He completed standard chemoradiation with temozolomide. He developed a recurrence in October 2011, and subsequently received Avastin. He had an additional recurrence and received an additional resection in June 2013. He was enrolled in a clinical trial, which was discontinued due to recurrence in March 2013. He was restarted on Avastin. His physician prescribed Optune for GBM treatment on April 3, 2013. He had a diagnosis of recurrent GBM and was on his third progression at the time of therapy. He tried all FDA-approved options for his recurrent GBM. At the time of therapy, Optune was FDA-approved for his specific condition. The NCCN Guidelines also recommended Optune for this indication, with a category 2B level of evidence and consensus.

The Appellant's representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The Appellant's representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

Principles of Law

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges ("ALJ's") within OMHA issue binding decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.*

For requests filed in calendar years 2010 through 2012, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible) and \$140.00 for calendar years 2013 through 2014. *See* §1869(b)(1)(E) of the Act, 74 Fed. Reg. 48976 (Sept. 2, 2009), 75 Fed. Reg. 58407 (Sept. 23, 2010), 76 Fed. Reg. 59138 (Sept. 23, 2011), 77 Fed. Reg. 59619 (Sept. 28, 2012), 78 Fed. Reg. 59702 (Sept. 27, 2013), 42 C.F.R. § 405.1006(b), and 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. Section 557 of the Administrative Procedure Act and 70 Fed. Reg. 36386 (June 23, 2005). *De novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. *See* 42 C.F.R. § 405.1018. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. *See* 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Social Security Act

Medicare Part B provides coverage to eligible beneficiaries for all or part of the cost of "medical and other health services," a term which is defined by the Act as including, among many other

things, durable medical equipment.” *Sections 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Social Security Act; 42 C.F.R. §410.10(h).*

No Medicare payment can be allowed for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member *Section 1862(a)(1)(A) of Title XVIII of the Social Security Act; 42 C.F.R. §411.15(k)(2).*

No payment can be made to the provider or another person unless such information, as may be necessary, has been furnished in support of the medical necessity of the claimed services in order to determine the amount due such provider or other individual. *Section 1833 of Title XVIII of the Social Security Act; 42 C.F.R. §424.5(a)(6).*

When Medicare coverage is precluded under Section 1862(a)(1)(A), i.e., the item was not reasonable and necessary, payment will be made, notwithstanding the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably be expected to know that the item was not covered. This provision is commonly referred to as the limitation of liability provision. *Section 1879 of Title XVIII of the Social Security Act, 42 C.F.R. §411.400.*

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than National Coverage Determinations, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also 42 C.F.R. §405.860.* However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals or local coverage determinations (“LCDs”). 42 C.F.R. § 405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs) or Center for Medicare Services (“CMS”) program guidance when applicable. There is no applicable LCD in the instant case.

Analysis

The amount in controversy is in excess of \$140.00. The QIC issued an unfavorable reconsideration decision on January 16, 2014. By correspondence received on February 28, 2014, the Appellant made a request for an ALJ hearing before OMHA. Therefore, the Appellant’s request was made in a timely manner and the claim satisfies the jurisdictional requirements for an ALJ Hearing before OMHA.

The QIC in its unfavorable decision stated, in part, as follows: “There is insufficient documentation to quantify the effects of the device for this beneficiary. No additional medical records have been submitted to explain why this particular beneficiary should be considered for this treatment. In addition, no documentation has been received to show the suggested manufacturer retail price for the service(s) billed. Based on the available documentation, payment cannot be allowed” (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on April 3, 2013, May 3, 2013, June 3, 2013 and July 3, 2013, and INE Insulated Transducer Arrays billed under miscellaneous DME accessory (A9900) on April 3, 2013 and May 1, 2013.

The Beneficiary has a medical history that includes right parietal GBM (Ex. 2). He underwent a total resection and then began chemotherapy and radiation treatment (*Id.*). His treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "*as a factor* in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment. In addition, the record indicates that after the Beneficiary initiated TTFT with the NovoTTF-100A system, his condition was deemed stable in June 2013.

The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had a diagnosis of recurrent GBM and was on his third progression at the time of therapy. He tried all FDA-approved options for his recurrent GBM. At the time of therapy, Optune was FDA-approved for his specific condition. The NCCN Guidelines also recommended Optune for this indication, with a category 2B level of evidence and consensus.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTFT has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. Since the NovoTTF-100A System at issue is medically reasonable and necessary, the NovoTTF-100A System transducer arrays is also covered under Section 1862(a)(7) of the Social Security Act. As such, Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399), and miscellaneous DME accessory (A9900) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Conclusions of Law

Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399), and miscellaneous DME accessory (A9900) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

AUG 23 2017

SO ORDERED

Dated:



Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of: NOVOCURE INC.	OMHA Appeal No.: 1-2426208701
Beneficiary:	Medicare: Part B
HICN: *****3605A	Before: Hon. Roberto M. Gutierrez U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, , received miscellaneous durable medical equipment (“DME”), NovoTTF-100A System (E1399) from the Appellant on April 5, 2013, May 5, 2013 and June 5, 2013, the dates of service at issue. The Appellant’s claim to Medicare was denied by National Government Services, a Medicare Administrative Contractor (“Contractor”), upon initial and redetermination. On October 24, 2013, C2C Solutions, Inc., a Medicare Qualified Independent Contractor (“QIC”), upheld the prior denials upon reconsideration review. By correspondence received on January 8, 2014, the Appellant made a timely request for an Administrative Law Judge (“ALJ”) hearing before the Office of Medicare Hearings and Appeals (“OMHA”). 42 C.F.R. § 405.1014(b)(1).

On July 27, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference. The Appellant’s additional evidence was excluded from the record as good cause was not found to admit the new evidence because the evidence was duplicative.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the dates of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on October 24, 2013 (*Id.*). By correspondence received on January 8, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: “The NovoTTF-100A system electric field generator billed with procedure code E1399 does not fall into any Medicare benefit category and therefore, is excluded from coverage. The claim is non-covered and will not be allowed” (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on April 5, 2013, May 5, 2013 and June 5, 2013.

The Beneficiary has a medical history that includes recurrent glioblastoma multiforme (“GBM”) (Ex. 2). He was diagnosed with malignant glioma (*Id.*). He underwent a total resection and then began chemotherapy and radiation treatment (*Id.*). He had radiographic progressive disease per MRI in May 2012 (*Id.*). On March 19, 2013, his treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy (“TTFT”) (*Id.*).

The Food and Drug Administration (“FDA”) approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

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The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary. The therapy was established and proven as an option for recurrent GBM through peer reviewed journals, clinical guidelines and is widely recognized in the field nationwide. GBM is an aggressive, primary brain cancer. Prior to Optune being FDA approved, patients had a life expectancy with treatment of about 12 to 15 months. A disease is labeled recurrent after a patient has progressed after initial therapy. A 1 year survival rate for a recurrent GBM patient is about 10%. When GBM recurs, about 20% of patients are eligible for a reoperation or an additional resection. Most patients are not eligible for additional radiation because they have already maxed out their radiation dose with the initial treatment. A chemotherapy regimen that has already been tried and failed is not an option when a tumor recurs or progresses post-treatment. As a result, recurrent GBM patients have very limited treatment options.

The Appellant's representative further testified that the Beneficiary was 21 years-old when he was diagnosed with a left insular oligodendroglioma in May 2007. He underwent subtotal resection and experienced significant complications from surgery due to aspiration during the

procedure, which resulted in 6 months of hospitalization and rehab to recover. He received radiation followed by 2 years of temozolomide, which was stopped in 2012. In May 2012, he developed a recurrence concerning for recurrent disease in a transformation to a high grade glioma. He was not a candidate for an additional surgical resection as a result of the significant complications he experienced in his initial resection surgery. He then received proton therapy followed by temozolomide and Avastin therapy. In May 2012, his MRI showed additional progression, and his regimen was switched to Avastin and carboplatin. He was then offered Optune as a last option to slow the progression of his disease, and he began treatment on April 5, 2013 at age 26. He had a recurrent, high grade glioma at the time his physician prescribed TTFT. As documented in the medical record, the physician believed this was the only treatment option not tried. He was 21 years old when first diagnosed with a brain tumor, and 26 years old when he started Optune as a last option to treat his recurrent, high grade glioma.

The Appellant's representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The Appellant's representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

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For requests filed in calendar years 2010 through 2012, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible) and \$140.00 for calendar years 2013 through 2014. *See* §1869(b)(1)(E) of the Act, 74 Fed. Reg. 48976 (Sept. 2, 2009), 75 Fed. Reg. 58407 (Sept. 23, 2010), 76 Fed. Reg. 59138 (Sept. 23, 2011), 77 Fed. Reg. 59619 (Sept. 28, 2012), 78 Fed. Reg. 59702 (Sept. 27, 2013), 42 C.F.R. § 405.1006(b), and 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. Section 557 of the Administrative Procedure Act and 70 Fed. Reg. 36386 (June 23, 2005). *De novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. *See* 42 C.F.R. § 405.1018. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. *See* 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Social Security Act

Medicare Part B provides coverage to eligible beneficiaries for all or part of the cost of "medical and other health services," a term which is defined by the Act as including, among many other

things, durable medical equipment.” *Sections 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Social Security Act; 42 C.F.R. §410.10(h).*

No Medicare payment can be allowed for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member *Section 1862(a)(1)(A) of Title XVIII of the Social Security Act; 42 C.F.R. §411.15(k)(2).*

No payment can be made to the provider or another person unless such information, as may be necessary, has been furnished in support of the medical necessity of the claimed services in order to determine the amount due such provider or other individual. *Section 1833 of Title XVIII of the Social Security Act; 42 C.F.R. §424.5(a)(6).*

When Medicare coverage is precluded under Section 1862(a)(1)(A), i.e., the item was not reasonable and necessary, payment will be made, notwithstanding the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably be expected to know that the item was not covered. This provision is commonly referred to as the limitation of liability provision. *Section 1879 of Title XVIII of the Social Security Act, 42 C.F.R. §411.400.*

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than National Coverage Determinations, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also 42 C.F.R. §405.860.* However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals or local coverage determinations (“LCDs”). 42 C.F.R. § 405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs) or Center for Medicare Services (“CMS”) program guidance when applicable. There is no applicable LCD in the instant case.

Analysis

The amount in controversy is in excess of \$140.00. The QIC issued an unfavorable reconsideration decision on October 24, 2013. By correspondence received on January 8, 2014, the Appellant made a request for an ALJ hearing before OMHA. Therefore, the Appellant’s request was made in a timely manner and the claim satisfies the jurisdictional requirements for an ALJ Hearing before OMHA.

The QIC in its unfavorable decision stated, in part, as follows: “The NovoTTF-100A system electric field generator billed with procedure code E1399 does not fall into any Medicare benefit category and therefore, is excluded from coverage. The claim is non-covered and will not be allowed” (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on April 5, 2013, May 5, 2013 and June 5, 2013.

The Beneficiary has a medical history that includes recurrent GBM (Ex. 2). He was diagnosed with malignant glioma (*Id.*). He underwent a total resection and then began chemotherapy and radiation treatment (*Id.*). He had radiographic progressive disease per MRI in May 2012 (*Id.*). On March 19, 2013, his treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category (*See* Ex 2). Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "*as a factor* in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment.

The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had a recurrent, high grade glioma at the time his physician prescribed TTFT. As documented in the medical record, the physician believed this was the only treatment option not tried. He had undergone subtotal resection and experienced significant complications from surgery due to aspiration during the procedure, which resulted in 6 months of hospitalization and rehab to recover. He was not a candidate for an additional surgical resection as a result of the significant complications he experienced in his initial resection surgery. He was 21 years old when first diagnosed with a brain tumor, and 26 years old when he started Optune as a last option to treat his recurrent, high grade glioma. At the time he utilized the therapy, Optune was FDA-approved for his specific condition. In addition, the NCCN Guidelines recommend Optune for this indication, with a category 2B level of evidence and consensus.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTFT has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. As such, Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Conclusions of Law

Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.


Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated:

AUG 23 2017


Hon. Roberto M. Gafierrez
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of: **NOVOCURE INC.**

OMHA Appeal No.: **1-2506558611**

Beneficiary:

Medicare: **Part B**

HICN: *******8471A**

Before: **Hon. Roberto M. Gutierrez**
U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, , received miscellaneous durable medical equipment ("DME"), NovoTTF-100A System (E1399) from the Appellant on July 1, 2013, and miscellaneous DME accessory (A9900) on August 5, 2013, the dates of service at issue. The Appellant's claim to Medicare was denied by NHIC, a Medicare Administrative Contractor ("Contractor"), upon initial and redetermination. On January 27, 2014, C2C Solutions, Inc., a Medicare Qualified Independent Contractor ("QIC"), upheld the prior denials upon reconsideration review. By correspondence received on February 24, 2014, the Appellant made a timely request for an Administrative Law Judge ("ALJ") hearing before the Office of Medicare Hearings and Appeals ("OMHA"). 42 C.F.R. § 405.1014(b)(1).

On July 27, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference. The Appellant's additional evidence was excluded from the record as good cause was not found to admit the new evidence because the evidence was duplicative.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399), and miscellaneous DME accessory (A9900) provided to the Beneficiary on the dates of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on January 27, 2014 (*Id.*). By correspondence received on February 24, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: "There is insufficient documentation to quantify the effects of the device for this beneficiary. No additional medical records have been submitted to explain why this particular beneficiary should be considered for this treatment. In addition, no documentation has been received to show the suggested manufacturer retail price for the service(s) billed" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on July 1, 2013, and a NovoTTF-100A System transducer arrays billed under miscellaneous DME accessory (A9900) on August 5, 2013.

The Beneficiary has a medical history that includes WHO grade III astrocytoma involving the left temporal lobe (Ex. 2). He underwent biopsy and then began temozolomide and radiation treatment (*Id.*). Despite this treatment, he was found to have progression of disease in February 2013 (*Id.*). He was then started on Avastin (*Id.*). On June 15, 2013, his treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy ("TTFT") (*Id.*). The record includes treatment notes from June 4, 2013, which indicate the Beneficiary initiated TTFT on May 1, 2013, and that his last MRI from May 28, 2013, showed stable disease (*Id.*).

The Food and Drug Administration ("FDA") approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed glioblastoma multiforme ("GBM"), following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population (*Id.*). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009 (*Id.*). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life (*Id.*).

The record includes a publication from the National Comprehensive Cancer Network ("NCCN") Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," which reflects that as of the date of the publication, December 21, 2012, alternating electric field

therapy was considered an effective treatment option for recurrent GBM and anaplastic gliomas, including anaplastic astrocytomas (*Id.*). Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment (*Id.*).

At the hearing, the Appellant's representative testified that Optune (which was previously known as the NovoTTF-100A system) is a portable, wearable device that delivers tumor treating fields, which are alternating electric fields, to the brain. The device consists of a portable, electric field generator connected to a portable battery that is connected to 4 insulated transducer arrays that are placed on the patient's scalp. The device generates electric currents that go through the transducer arrays, which creates the tumor treating fields. In 2013, after receiving billing rights from CMS, the Appellant billed the device under 2 components: (1) the electric field generator, billed under E1399; and (2) the insulated transducer arrays, billed as a DME supply under miscellaneous code A9900. In 2014, effective January 1, 2014, CMS issued two HCPCS codes for the NovoTTF-100A system: E0766 for the device; and A4555 for the transducer arrays. At that time, CMS designated the therapy as DME requiring frequent and substantial servicing.

The therapy delivers alternating electric fields to the brain. The electric fields disrupt the formation of the mitotic spindle in the dividing cancer cell. The therapy is similar to taxing chemotherapy insofar as it inhibits the formation of the mitotic spindle, which leads to program cell death. The therapy does not affect non-dividing cells and is frequency-tuned specifically to GBM cells.

The therapy was approved by the FDA in 2011 under the pre-market approval pathway, which is the most stringent device approval pathway. Only 2% of medical devices are approved through this pathway. That approval was based on a randomized controlled trial in recurrent GBM of 243 patients that compared using Optune by itself to physician-choice chemotherapy. The FDA concluded in its initial approval that the NovoTTF-100A system treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness, and a better quality of life compared to chemotherapy in the control arm of the study. This trial was published in the *European Journal of Cancer* in 2012, which is a CMS-recognized medical journal. According to the Appellant, Optune is included in the NCCN Guidelines with a consensus 2B recommendation for recurrent GBM and a 2A uniform consensus recommendation for newly diagnosed GBM in combination with temozolomide.

The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary. The therapy was established and proven as an option for recurrent GBM through peer reviewed journals, clinical guidelines and is widely recognized in the field nationwide. GBM is an aggressive, primary brain cancer. Prior to Optune being FDA approved, patients had a life expectancy with treatment of about 12 to 15 months. A disease is labeled recurrent after a patient has progressed after initial therapy. A 1 year survival rate for a recurrent GBM patient is about 10%. When GBM recurs, about 20% of patients are eligible for a reoperation or an additional resection. Most patients are not eligible for additional radiation because they have already maxed out their radiation dose with the initial treatment. A chemotherapy regimen that has already been tried and failed is not an option when a tumor recurs or progresses post-treatment. As a result, recurrent GBM patients have very limited treatment options.

The Appellant's representative further testified that the Beneficiary was diagnosed with WHO grade III astrocytoma involving the left temporal lobe in May 2013. He underwent a biopsy, which confirmed an anaplastic astrocytoma. An astrocytoma, like GBM, is a primary brain cancer and is rare. Astrocytoma tumors are even rarer than GBM tumors. Diagnoses of this type of tumor and the grade of tumor are made based on the type of cell seen in histology and biopsy analysis. Grade I tumors are benign, grade II tumors are intermediate, and grade III and IV are malignant tumors. A grade III anaplastic astrocytoma typically grows at a faster pace than lower grade astrocytomas but not as quickly as a grade IV astrocytoma or glioblastoma. Tumors that progress are typically classified as grade IV astrocytoma or GBM tumors. Because anaplastic astrocytomas are so rare, very few studies have focused specifically on anaplastic astrocytoma. Further, there are no FDA-approved treatment options for recurrent anaplastic astrocytoma. For a newly diagnosed astrocytoma patient, there is only one FDA approved therapy, and that is temozolomide. The Beneficiary was diagnosed with a grade III anaplastic astrocytoma. Following that diagnosis, he completed standard chemoradiation with temozolomide. After initial treatment, he developed recurrence in February 2013, and was started on Avastin. There are no FDA-approved treatment options for recurrent anaplastic astrocytoma. Temozolomide chemotherapy had been tried and exhausted, so it was not an option in this case. Following treatment with Avastin, he had further recurrence and his treating physician at that point prescribed Optune in combination with Avastin. He began this therapy on May 1, 2013. A grade III anaplastic astrocytoma that progresses to grade IV is a recurrent GBM tumor. When a patient has recurrent anaplastic astrocytoma, biopsies are typically not performed for recurrence unless it is critically necessary to do so as it can cause pain and create risks to the patient. Although there are no FDA-approved treatments for recurrent anaplastic astrocytoma tumors, certain clinical guidelines, such as the NCCN Guidelines, consider several types of recurrent brain tumors under the same general pathway, including recurrent GBM and recurrent anaplastic astrocytoma tumors. In this case, the Beneficiary's medical record reflects his anaplastic astrocytoma and recurrent anaplastic astrocytoma diagnoses, as well as the treating physician statement that he had a history of and had been diagnosed with GBM for recurrent tumor. There are no other FDA approved treatments for him. While the Beneficiary's diagnosis is a grade III anaplastic astrocytoma and not a grade IV, patients with recurrence are typically treated the same as recurrent GBM patients.

The Appellant's representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The Appellant's representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that

Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

Principles of Law

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges ("ALJ's") within OMHA issue binding decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.*

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The Beneficiary has a medical history that includes WHO grade III astrocytoma involving the left temporal lobe (Ex. 2). He underwent biopsy and then began temozolomide and radiation treatment (*Id.*). Despite this treatment, he was found to have progression of disease in February 2013 (*Id.*). He was then started on Avastin (*Id.*). On June 15, 2013, his treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*). The record includes treatment notes from June 4, 2013, which indicate the Beneficiary initiated TTFT on May 1, 2013, and that his last MRI from May 28, 2013, showed stable disease (*Id.*).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category (*See* Ex. 2). Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS may consider for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "as a factor in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and anaplastic gliomas, including anaplastic astrocytomas, and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM and anaplastic gliomas, including anaplastic astrocytomas. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment.

The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had a diagnosis of WHO grade III anaplastic astrocytoma and had recurrence at the time of therapy. He tried all FDA-approved options for his recurrent anaplastic astrocytoma. A grade III anaplastic astrocytoma that progresses to grade IV is a recurrent GBM tumor. Although there are no FDA-approved treatments for recurrent anaplastic astrocytoma tumors, certain clinical guidelines, such as the NCCN Guidelines, consider several types of recurrent brain tumors under the same general pathway, including recurrent GBM and recurrent anaplastic astrocytoma tumors. In this case, the Beneficiary's medical record reflects his anaplastic astrocytoma and recurrent anaplastic astrocytoma diagnoses, as well as the treating physician statement that he had a history of and had been diagnosed with GBM for recurrent tumor. There are no other FDA approved treatments for him. While the Beneficiary's diagnosis is a grade III anaplastic astrocytoma and not a grade IV, patients with recurrence are typically treated the same as recurrent GBM patients. The record also indicates that after the Beneficiary initiated TTFT with the NovoTTF-100A system, his last MRI from May 28, 2013, showed stable disease.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTFT has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. Since the NovoTTF-100A System at issue is medically reasonable and necessary, the NovoTTF-100A System transducer arrays is also covered under Section 1862(a)(7) of the Social Security Act. As such, Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399), and miscellaneous DME accessory (A9900) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Conclusions of Law

Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399), and miscellaneous DME accessory (A9900) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated:

AUG 23 2017



Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of: **NOVOCURE INC.**

OMHA Appeal No.: **1-2426208806**

Beneficiary:

Medicare: **Part B**

HICN: *******1134A**

Before: **Hon. Roberto M. Gutierrez**
U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, , received miscellaneous durable medical equipment ("DME"), NovoTTF-100A System (E1399) from the Appellant on May 10, 2013 and June 10, 2013, the dates of service at issue. The Appellant's claim to Medicare was denied by National Government Services, a Medicare Administrative Contractor ("Contractor"), upon initial and redetermination. On November 13, 2013, C2C Solutions, Inc., a Medicare Qualified Independent Contractor ("QIC"), upheld the prior denials upon reconsideration review. By correspondence received on January 8, 2014, the Appellant made a timely request for an Administrative Law Judge ("ALJ") hearing before the Office of Medicare Hearings and Appeals ("OMHA"). 42 C.F.R. § 405.1014(b)(1).

On July 25, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference. The Appellant's additional evidence was excluded from the record as good cause was not found to admit the new evidence because the evidence was duplicative.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the dates of service at issue, and, if not, who is responsible for the non-covered charges?

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Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on November 13, 2013 (*Id.*). By correspondence received on January 8, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: "The NovoTTF-100A system electric field generator billed with procedure code E1399 does not fall into any Medicare benefit category and therefore, is excluded from coverage. The claim is non-covered and will not be allowed" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on May 10, 2013 and June 10, 2013.

The Beneficiary has a medical history that includes recurrent glioblastoma multiforme ("GBM") (Ex. 2). She had malignant glioma and was diagnosed with oligodendroglioma (*Id.*). She underwent chemotherapy and radiation treatment (*Id.*). She had demonstrated both clinical and radiographic evidence of progressive disease on April 25, 2013 (*Id.*). On May 2, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy ("TTFT") (*Id.*).

The Food and Drug Administration ("FDA") approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population (Ex. 1). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009 (Ex. 2). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life (*Id.*).

The record includes a publication from the National Comprehensive Cancer Network ("NCCN") Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," which reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM (*Id.*). Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment (*Id.*).

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At the hearing, the Appellant testified that the Beneficiary was diagnosed with a malignant glioma on September 10, 2002 after CT guided needle biopsy. Progression was identified in 2013, with MRI confirmation and worsening of symptoms, including headaches and visual disturbances. She received Tomo radiation therapy, multiple cycles of CCNU, and procarbazine but was discontinued due to nausea. She subsequently received thalidomide in 2008 and 2009. She experienced recurrence with clinical worsening symptoms in 2012. Upon review of the treatment options, the physician determined that the NovoTTF-100A system (also known as Optune®) was the only treatment the Beneficiary had not tried and further chemotherapy was not an option due to the side effects of her medication. The Appellant testified that documentation in the medical record shows the Beneficiary has a history of leukopenia secondary to chemotherapy as well as chronic nausea. She began Optune on May 10, 2013, and received the device as directed by her physician under the FDA label. She had a recurrent malignant glioma and was on her fourth progression at the time of therapy. She had severe complications from her chemotherapy, including leukopenia and nausea, and she had exhausted all FDA approved options at the time her physician prescribed Optune. The Appellant testified that at the time of therapy, Optune was FDA-approved for her specific condition, and the NCCN Clinical Guidelines recommended Optune for this indication with a category 2B level of evidence and consensus at the time of treatment.

According to the Appellant, Optune (previously known as the NovoTTF-100A system), was FDA approved in 2011 for patients diagnosed with recurrent GBM. This approval was based on a large, randomized trial of 243 patients that compared using Optune as a modal therapy to those using physician-choice chemotherapy. The FDA concluded that the NovoTTF-100A treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness, and better quality of life compared to the chemotherapy in the control arm of this study. The FDA approved the NovoTTF-100A system under the FDA pre-market approval process, where both safety and effectiveness in a randomized study need to be shown in order to get approval through that pathway. The Appellant maintained that the FDA's own website and materials refer to pre-market approval as the most stringent form of approval for devices. This trial was published in the *European Journal of Cancer*, which is a CMS-recognized journal, and included in the record. According to the Appellant, Optune is included in the NCCN Guidelines with a consensus 2B recommendation for recurrent GBM and a 2A uniform consensus recommendation for newly diagnosed GBM in combination with temozolomide. The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage.

The Appellant testified that this Beneficiary's diagnosis of recurrent high grade glioma has few proven treatment options. She was on her fourth progression and had failed all standard of care treatments at the time she began Optune. Her physician made a judgment that this therapy was the most appropriate option at the time of treatment. The standard of care NCCN Guidelines recommend this treatment for recurrent GBM and they did so at the time she was treated. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary.

The Appellant's representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The

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Appellant's representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

Principles of Law

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. See 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges ("ALJ's") within OMHA issue binding decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.*

For requests filed in calendar years 2010 through 2012, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible) and \$140.00 for calendar years 2013 through 2014. See §1869(b)(1)(E) of the Act, 74 Fed. Reg. 48976 (Sept. 2, 2009), 75 Fed. Reg. 58407 (Sept. 23, 2010), 76 Fed. Reg. 59138 (Sept. 23, 2011), 77 Fed. Reg. 59619 (Sept. 28, 2012), 78 Fed. Reg. 59702 (Sept. 27, 2013), 42 C.F.R. § 405.1006(b), and 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at

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an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. Section 557 of the Administrative Procedure Act and 70 Fed. Reg. 36386 (June 23, 2005). *De novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). See e.g., Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; see also 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into in the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. See 42 C.F.R. § 405.1018. See also 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. See 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Social Security Act

Medicare Part B provides coverage to eligible beneficiaries for all or part of the cost of "medical and other health services," a term which is defined by the Act as including, among many other things, durable medical equipment." Sections 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Social Security Act; 42 C.F.R. §410.10(h).

No Medicare payment can be allowed for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. Section 1862(a)(1)(A) of Title XVIII of the Social Security Act; 42 C.F.R. §411.15(k)(2).

No payment can be made to the provider or another person unless such information, as may be necessary, has been furnished in support of the medical necessity of the claimed services in order to determine the amount due such provider or other individual. Section 1833 of Title XVIII of the Social Security Act; 42 C.F.R. §424.5(a)(6).

When Medicare coverage is precluded under Section 1862(a)(1)(A), i.e., the item was not reasonable and necessary, payment will be made, notwithstanding the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could

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reasonably be expected to know that the item was not covered. This provision is commonly referred to as the limitation of liability provision. *Section 1879 of Title XVIII of the Social Security Act, 42 C.F.R. §411.400.*

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than National Coverage Determinations, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also 42 C.F.R. §405.860.* However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals or local coverage determinations ("LCDs"). 42 C.F.R. § 405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs) or Center for Medicare Services ("CMS") program guidance when applicable. There is no applicable LCD in the instant case.

Analysis

The amount in controversy is in excess of \$140.00. The QIC issued an unfavorable reconsideration decision on November 13, 2013. By correspondence received on January 8, 2014, the Appellant made a request for an ALJ hearing before OMHA. Therefore, the Appellant's request was made in a timely manner and the claim satisfies the jurisdictional requirements for an ALJ Hearing before OMHA.

The QIC in its unfavorable decision stated, in part, as follows: "The NovoTTF-100A system electric field generator billed with procedure code E1399 does not fall into any Medicare benefit category and therefore, is excluded from coverage. The claim is non-covered and will not be allowed" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on May 10, 2013 and June 10, 2013.

Beneficiary has a medical history that includes recurrent GBM (Ex. 2). She had malignant glioma and was diagnosed with oligodendroglioma (*Id.*). She underwent chemotherapy and radiation treatment (*Id.*). She had demonstrated both clinical and radiographic evidence of progressive disease on April 25, 2013 (*Id.*). On May 2, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

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As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category (See Ex 1). Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "*as a factor* in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment.

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The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had a diagnosis of recurrent high grade glioma, which has few proven treatment options. She was on her fourth progression and had failed all standard of care treatments at the time she began Optune. She had severe complications from her chemotherapy, including leukopenia and nausea. Her physician made a judgment that this therapy was the most appropriate option at the time of treatment. At the time of therapy, Optune was FDA-approved for her specific condition. The standard of care NCCN Guidelines recommend this treatment for recurrent GBM and they did so at the time she was treated.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTF-100A has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. As such, Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Conclusions of Law

Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the dates of service at issue, and the Appellant is entitled to the same.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated:

JUL 31 2017


Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida**

Appeal of: NOVOCURE INC.	OMHA Appeal No.: 1-2450006941
Beneficiary:	Medicare: Part B
HICN: *****0878A	Before: Hon. Roberto M. Gutierrez U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, , received miscellaneous durable medical equipment (“DME”), NovoTTF-100A System (E1399) from the Appellant on May 9, 2013, the date of service at issue. The Appellant’s claim to Medicare was denied by CGS Administrators, LLC, a Medicare Administrative Contractor (“Contractor”), upon initial and redetermination. On November 22, 2013, C2C Solutions, Inc., a Medicare Qualified Independent Contractor (“QIC”), upheld the prior denials upon reconsideration review. By correspondence received on January 17, 2014, the Appellant made a timely request for an Administrative Law Judge (“ALJ”) hearing before the Office of Medicare Hearings and Appeals (“OMHA”). 42 C.F.R. § 405.1014(b)(1).

On July 25, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference. The Appellant’s additional evidence was excluded from the record as good cause was not found to admit the new evidence because the evidence was duplicative.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the date of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on November 22, 2013 (*Id.*). By correspondence received on January 17, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: “There is a NOVOTTF-100A System order form submitted with a diagnosis of brain cancer. The documentation submitted does not indicate that the NOVOTTF-100A System falls within a Medicare benefit category. Based on the available documentation, the requirements of the Medicare Benefit Policy Manual have not been met” (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on May 9, 2013.

Beneficiary has a medical history that includes recurrent left posterior temporoparietal glioblastoma multiforme (“GBM”) (Ex. 2). She underwent a left temporal-occipital craniotomy with resection and then began chemotherapy and radiation treatment (*Id.*). On May 9, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy (“TTFT”) (*Id.*).

The Food and Drug Administration (“FDA”) approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

The Appellant submitted a letter of medical necessity from the Beneficiary’s treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population (*Id.*). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009 (*Id.*). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life (*Id.*).

The record includes a publication from the National Comprehensive Cancer Network (“NCCN”) Clinical Practice Guidelines in Oncology entitled, “Central Nervous System Cancers,” which reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM (*Id.*). Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment (*Id.*).

At the hearing, the Appellant's representative testified that the Beneficiary was diagnosed with a left occipital GBM in May 2012 and received a surgical resection with histological confirmation of GBM. She received standard chemo radiation with temozolomide in June and July 2012, followed by maintenance temozolomide. Progression was identified in November 2012, and she was enrolled in a clinical trial but was discontinued after she showed progression. She was enrolled in a second clinical trial but that was discontinued due to worsening thrombocytopenia 4-5 weeks post treatment. She was later admitted in February 2013 with cerebral edema. In April 2013, she presented with progressive refractory disease and poor tolerance to chemotherapy medications. Based on this information, the physician prescribed the NovoTTF-100A system (also known as Optune®). She began Optune on May 9, 2013, and received the device as directed by her physician. The Appellant testified that at the time of therapy, Optune was FDA-approved for her specific condition, and the NCCN Clinical Guidelines recommended Optune for this indication with a category 2B level of evidence and consensus at the time of treatment.

According to the Appellant, Optune (previously known as the NovoTTF-100A system), was FDA approved in 2011 for patients diagnosed with recurrent GBM. This approval was based on a large, randomized trial of 243 patients that compared using Optune as a modal therapy to those using physician-choice chemotherapy. The FDA concluded that the NovoTTF-100A treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness, and better quality of life compared to the chemotherapy in the control arm of this study. The FDA approved the NovoTTF-100A system under the FDA pre-market approval process, where both safety and effectiveness in a randomized study need to be shown in order to get approval through that pathway. The Appellant maintained that the FDA's own website and materials refer to pre-market approval as the most stringent form of approval for devices. This trial was published in the *European Journal of Cancer*, which is a CMS-recognized journal, and included in the record. According to the Appellant, Optune is included in the NCCN Guidelines with a consensus 2B recommendation for recurrent GBM and a 2A uniform consensus recommendation for newly diagnosed GBM in combination with temozolomide. The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage.

The Appellant testified that this beneficiary had recurrent GBM and was on her third progression at the time of therapy. She could not tolerate chemotherapy medications due to her thrombocytopenia. There were no other FDA approved treatment options for her at the time her physician prescribed Optune. At the time of therapy, Optune was FDA-approved for her specific condition and included in the NCCN Guidelines with a category 2B level of evidence and consensus. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary.

The Appellant's representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The Appellant's representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered

under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

Regarding the Contractor's finding that the medical record does not include documentation to show the suggested manufacturer retail price for the services billed, the Appellant's representative pointed out that invoices are included with every claim and every appeal, and those invoices do provide documentation of the suggested retail price.

Principles of Law

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges ("ALJ's") within OMHA issue binding decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.*

For requests filed in calendar years 2010 through 2012, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible) and \$140.00 for calendar years 2013 through 2014. *See* §1869(b)(1)(E) of the Act, 74 Fed. Reg. 48976 (Sept. 2, 2009), 75 Fed. Reg. 58407 (Sept. 23, 2010), 76 Fed. Reg. 59138 (Sept. 23, 2011), 77 Fed. Reg. 59619 (Sept. 28, 2012), 78 Fed. Reg. 59702 (Sep. 27, 2013), 42 C.F.R. § 405.1006(b), and 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at

an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. Section 557 of the Administrative Procedure Act and 70 Fed. Reg. 36386 (June 23, 2005). *De novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into in the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. *See* 42 C.F.R. § 405.1018. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. *See* 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Social Security Act

Medicare Part B provides coverage to eligible beneficiaries for all or part of the cost of “medical and other health services,” a term which is defined by the Act as including, among many other things, durable medical equipment.” *Sections 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Social Security Act; 42 C.F.R. §410.10(h).*

No Medicare payment can be allowed for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member *Section 1862(a)(1)(A) of Title XVIII of the Social Security Act; 42 C.F.R. §411.15(k)(2).*

No payment can be made to the provider or another person unless such information, as may be necessary, has been furnished in support of the medical necessity of the claimed services in order to determine the amount due such provider or other individual. *Section 1833 of Title XVIII of the Social Security Act; 42 C.F.R. §424.5(a)(6).*

When Medicare coverage is precluded under Section 1862(a)(1)(A), i.e., the item was not reasonable and necessary, payment will be made, notwithstanding the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could

reasonably be expected to know that the item was not covered. This provision is commonly referred to as the limitation of liability provision. *Section 1879 of Title XVIII of the Social Security Act, 42 C.F.R. §411.400.*

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than National Coverage Determinations, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. §405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals or local coverage determinations (“LCDs”). 42 C.F.R. § 405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs) or Center for Medicare Services (“CMS”) program guidance when applicable. There is no applicable LCD in the instant case.

Analysis

The amount in controversy is in excess of \$140.00. The QIC issued an unfavorable reconsideration decision on November 22, 2013. By correspondence received on January 17, 2014, the Appellant made a request for an ALJ hearing before OMHA. Therefore, the Appellant’s request was made in a timely manner and the claim satisfies the jurisdictional requirements for an ALJ Hearing before OMHA.

The QIC in its unfavorable decision stated, in part, as follows: “There is a NOVOTTF-100A System order form submitted with a diagnosis of brain cancer. The documentation submitted does not indicate that the NOVOTTF-100A System falls within a Medicare benefit category. Based on the available documentation, the requirements of the Medicare Benefit Policy Manual have not been met” (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on May 9, 2013.

The Beneficiary has a medical history that includes recurrent left posterior temporoparietal GBM (Ex. 2). She underwent a left temporal-occipital craniotomy with resection and then began chemotherapy and radiation treatment (*Id.*). On May 9, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category (*See Ex 2*). Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "*as a factor* in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment.

The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had recurrent GBM and was on her third progression at the time of therapy. She could not tolerate chemotherapy medications due to her thrombocytopenia. There were no other FDA approved treatment options for her at the time her physician prescribed Optune. At the time of therapy, Optune was FDA-approved for her specific condition and included in the NCCN Guidelines with a category 2B level of evidence and consensus.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTFT has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. As such, Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the date of service at issue, and the Appellant is entitled to the same.

Conclusions of Law

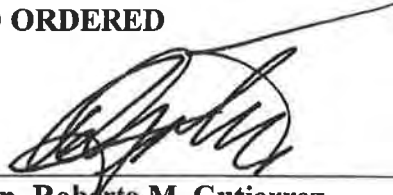
Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the date of service at issue, and the Appellant is entitled to the same.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

AUG 25 2017

SO ORDERED



Dated:

Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida**

Appeal of: **NOVOCURE INC.**

OMHA Appeal No.: **1-2426208625**

Beneficiary:

Medicare: **Part B**

HICN: *******4257A**

Before: **Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge**

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, received miscellaneous durable medical equipment ("DME"), NovoTTF-100A System (E1399) from the Appellant on May 23, 2013, the date of service at issue. The Appellant's claim to Medicare was denied by National Government Services, a Medicare Administrative Contractor ("Contractor"), upon initial and redetermination. On November 14, 2013, C2C Solutions, Inc., a Medicare Qualified Independent Contractor ("QIC"), upheld the prior denials upon reconsideration review. By correspondence received on January 8, 2014, the Appellant made a timely request for an Administrative Law Judge ("ALJ") hearing before the Office of Medicare Hearings and Appeals ("OMHA"). 42 C.F.R. § 405.1014(b)(1).

On July 25, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference. The Appellant's additional evidence was excluded from the record as good cause was not found to admit the new evidence because the evidence was duplicative.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the date of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on November 14, 2013 (*Id.*). By correspondence received on January 8, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: "In this instance, the submitted documentation does not serve a medical purpose. As such, Medicare guidelines have not been met. Therefore, payment cannot be effected for the NovoTTF-100A system at issue" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on May 23, 2013.

The Beneficiary has a medical history that includes recurrent left hemisphere glioblastoma multiforme ("GBM") (Ex. 2). She underwent a craniotomy with resection and then began chemotherapy and radiation treatment (*Id.*). She had radiographic progressive disease per MRI dated January 16, 2013 and April 17, 2013 (*Id.*). On May 16, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy ("TTFT") (*Id.*). The Beneficiary passed away on July 29, 2013 (Ex. 4).

The Food and Drug Administration ("FDA") approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (Ex. 2). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population (Ex. 1). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009 (Ex. 2). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life (*Id.*).

The record includes a publication from the National Comprehensive Cancer Network ("NCCN") Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," which reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM (*Id.*). Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment (*Id.*).

At the hearing, the Appellant testified that the Beneficiary was diagnosed with a left GBM in September 2011 and received a surgical resection on September 23, 2011, followed by a second

resection in October 2011. She completed standard chemo radiation in December 2011, and progression was identified in February 2012, at which time she underwent 23 Avastin infusions that were completed in January 2013. Progression was identified in January 2013. She underwent a third resection in April 2013. The Beneficiary began the NovoTTF-100A system (also known as Optune®) on May 23, 2013, and received the device as directed by her physician under the FDA labeling. Per her History & Physical (“H&P”), she tolerated treatment well and had minimal skin irritation and used the device at least 18 hours a day. In terms of her clinical situation, she had recurrent GBM and was on her third progression at the time of therapy. She had exhausted all FDA approved treatment options at the time her physician prescribed Optune. The Appellant testified that at the time of therapy, Optune was FDA-approved for her specific condition, and the NCCN Clinical Guidelines recommended Optune for this indication with a category 2B level of evidence and consensus at the time of treatment.

According to the Appellant, Optune (previously known as the NovoTTF-100A system), was FDA approved in 2011 for patients diagnosed with recurrent GBM. This approval was based on a large, randomized trial of 243 patients that compared using Optune as a modal therapy to those using physician-choice chemotherapy. The FDA concluded that the NovoTTF-100A treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness, and better quality of life compared to the chemotherapy in the control arm of this study. The FDA approved the NovoTTF-100A system under the FDA pre-market approval process, where both safety and effectiveness in a randomized study need to be shown in order to get approval through that pathway. The Appellant maintained that the FDA’s own website and materials refer to pre-market approval as the most stringent form of approval for devices. This trial was published in the *European Journal of Cancer*, which is a CMS-recognized journal, and included in the record. According to the Appellant, Optune is included in the NCCN Guidelines with a consensus 2B recommendation for recurrent GBM and a 2A uniform consensus recommendation for newly diagnosed GBM in combination with temozolomide. The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage.

The Appellant testified that this beneficiary had a diagnosis of recurrent GBM, an aggressive brain cancer with few proven treatment options. She was on her third progression and had failed all standard of care treatments at the time she began Optune. She used the device as directed by her physician and experienced minimal toxicity with treatment. The standard of care NCCN Guidelines recommend this treatment for recurrent GBM and they did so at the time she was treated. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary.

The Appellant’s representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The Appellant’s representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is

not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

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Analysis

The amount in controversy is in excess of \$140.00. The QIC issued an unfavorable reconsideration decision on November 14, 2013. By correspondence received on January 8, 2014, the Appellant made a request for an ALJ hearing before OMHA. Therefore, the Appellant’s request was made in a timely manner and the claim satisfies the jurisdictional requirements for an ALJ Hearing before OMHA.

The QIC in its unfavorable decision stated, in part, as follows: “In this instance, the submitted documentation does not serve a medical purpose. As such, Medicare guidelines have not been met. Therefore, payment cannot be effected for the NovoTTF-100A system at issue” (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on May 23, 2013.

The 67 year-old Beneficiary has a medical history that includes recurrent left hemisphere GBM (Ex. 2). She underwent a craniotomy with resection and then began chemotherapy and radiation treatment (*Id.*). She had radiographic progressive disease per MRI dated January 16, 2013 and April 17, 2013 (*Id.*). On May 16, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*). The Beneficiary passed away on July 29, 2013 (Ex. 4).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (Ex. 2). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category (*See Ex 1*). Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "*as a factor* in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment.

The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had a diagnosis of recurrent GBM. She was on her third progression and had failed all standard of care treatments at the time she began Optune. She had exhausted all FDA approved treatment options at the time her physician prescribed Optune. At the time of therapy, Optune was FDA-approved for her specific condition. She used the device as directed by her physician and experienced minimal toxicity with treatment. Per her H&P, she tolerated treatment well and had minimal skin irritation and used the device at least 18 hours a day. The standard of care NCCN Guidelines recommend this treatment for recurrent GBM and they did so at the time she was treated.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTFT has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. As such, Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the date of service at issue, and the Appellant is entitled to the same.

Conclusions of Law

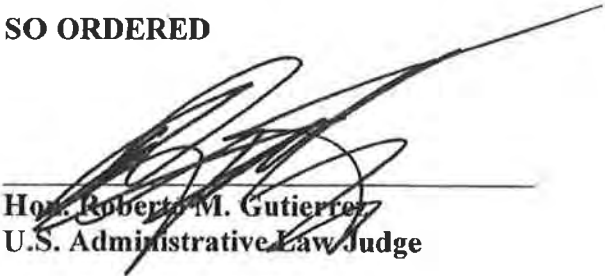
Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the date of service at issue, and the Appellant is entitled to the same.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated: **AUG 25 2017**


Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida**

Appeal of: **NOVOCURE INC.**

OMHA Appeal No.: **1-2426208663**

Beneficiary:

Medicare: **Part B**

HICN: *******1499A**

Before: **Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge**

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, , received miscellaneous durable medical equipment (“DME”), NovoTTF-100A System (E1399) from the Appellant on May 29, 2013, the date of service at issue. The Appellant’s claim to Medicare was denied by Noridian Healthcare Solutions, a Medicare Administrative Contractor (“Contractor”), upon initial and redetermination. On November 8, 2013, C2C Solutions, Inc., a Medicare Qualified Independent Contractor (“QIC”), upheld the prior denials upon reconsideration review. By correspondence received on January 8, 2014, the Appellant made a timely request for an Administrative Law Judge (“ALJ”) hearing before the Office of Medicare Hearings and Appeals (“OMHA”). 42 C.F.R. § 405.1014(b)(1).

On July 27, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference. The Appellant’s additional evidence was excluded from the record as good cause was not found to admit the new evidence because the evidence was duplicative.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the date of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on November 8, 2013 (*Id.*). By correspondence received on January 8, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: "The documentation submitted includes a signed and dated physician order for E1399-RR. However, there were no medical notes submitted for follow up for recurrent glioblastoma that support the need for the item billed. As a result, no payment will be allowed for the item billed as there is insufficient documentation from the patient's medical record to support the medical necessity for a NovoTTF-100A System" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on May 29, 2013.

The Beneficiary has a medical history that includes recurrent glioblastoma multiforme ("GBM") (Ex. 2). He had a gross total resection on February 4, 2010, and subsequently underwent chemotherapy and radiation treatment (*Id.*). He had disease progression found on imaging in February 2011 (*Id.*). He was on bevacizumab from March 2011 until April 2012 (*Id.*). He developed another nodule in the resection bed on December 6, 2012, and was referred to radiation (*Id.*). He had another disease progression in May 2013 (*Id.*). On May 14, 2013, his treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy ("TTFT") (*Id.*). The record includes a treatment note from August 20, 2013, which indicates the Beneficiary initiated Novo TTF in May 2013 and that an MRI from August 19, 2013, showed treatment response with overall decreased enhancement (*Id.*). The physician opined the Beneficiary was much improved clinically (*Id.*).

The Food and Drug Administration ("FDA") approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population (*Id.*). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009 (*Id.*). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life (*Id.*).

The record includes a publication from the National Comprehensive Cancer Network (“NCCN”) Clinical Practice Guidelines in Oncology entitled, “Central Nervous System Cancers,” which reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM (*Id.*). Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment (*Id.*).

At the hearing, the Appellant’s representative testified that Optune (which was previously known as the NovoTTF-100A system) is a portable, wearable device that delivers tumor treating fields, which are alternating electric fields, to the brain. The device consists of a portable, electric field generator connected to a portable battery that is connected to 4 insulated transducer arrays that are placed on the patient’s scalp. The device generates electric currents that go through the transducer arrays, which creates the tumor treating fields. In 2013, after receiving billing rights from CMS, the Appellant billed the device under 2 components: (1) the electric field generator, billed under E1399; and (2) the insulated transducer arrays, billed as a DME supply under miscellaneous code A9900. In 2014, effective January 1, 2014, CMS issued two HCPCS codes for the NovoTTF-100A system: E0766 for the device; and A4555 for the transducer arrays. At that time, CMS designated the therapy as DME requiring frequent and substantial servicing.

The therapy delivers alternating electric fields to the brain. The electric fields disrupt the formation of the mitotic spindle in the dividing cancer cell. The therapy is similar to taxing chemotherapy insofar as it inhibits the formation of the mitotic spindle, which leads to program cell death. The therapy does not affect non-dividing cells and is frequency-tuned specifically to GBM cells.

The therapy was approved by the FDA in 2011 under the pre-market approval pathway, which is the most stringent device approval pathway. Only 2% of medical devices are approved through this pathway. That approval was based on a randomized controlled trial in recurrent GBM of 243 patients that compared using Optune by itself to physician-choice chemotherapy. The FDA concluded in its initial approval that the NovoTTF-100A system treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness, and a better quality of life compared to chemotherapy in the control arm of the study. This trial was published in the *European Journal of Cancer* in 2012, which is a CMS-recognized medical journal. According to the Appellant, Optune is included in the NCCN Guidelines with a consensus 2B recommendation for recurrent GBM and a 2A uniform consensus recommendation for newly diagnosed GBM in combination with temozolomide.

The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary. The therapy was established and proven as an option for recurrent GBM through peer reviewed journals, clinical guidelines and is widely recognized in the field nationwide. GBM is an aggressive, primary brain cancer. Prior to Optune being FDA approved, patients had a life expectancy with treatment of about 12 to 15 months. A disease is labeled recurrent after a patient has progressed after initial therapy. A 1 year survival rate for a recurrent GBM patient is about 10%. When GBM recurs, about 20% of patients are eligible for a reoperation or an additional resection. Most patients are not eligible for additional radiation because they have already maxed out their radiation dose with the initial treatment. A

chemotherapy regimen that has already been tried and failed is not an option when a tumor recurs or progresses post-treatment. As a result, recurrent GBM patients have very limited treatment options.

The Appellant's representative further testified that the Beneficiary was diagnosed with GBM in January 2010 after developing slurred speech and word finding difficulties following a car accident. Imaging noted a mass in his brain, and he underwent a gross total resection in February 2010. He completed standard chemoradiation with temozolomide and he developed a recurrence in March 2011, and received bevacizumab through April 2012. He had a heart attack, which resulted in lowering the dose of Avastin and restarting 4 months after his myocardial infarction. He developed further recurrence in September 2012 and underwent stereotactic radiosurgery. The physician offered Optune to this patient, which he chose, because he wanted to preserve his quality of life. He had recurrent GBM and was on his second progression at the time of therapy. He had tried all other FDA approved options for his recurrent GBM. As noted in the clinical record, he had serious side effects from chemotherapy and his previous heart attack was a risk factor to restart bevacizumab. At the time of his therapy, the FDA had approved Optune for his specific condition, and the NCCN Guidelines had recommended this therapy with a level 2B evidence and consensus.

The Appellant's representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The Appellant's representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

Principles of Law

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for

hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act (“the Act”) section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges (“ALJ’s”) within OMHA issue binding decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.*

For requests filed in calendar years 2010 through 2012, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible) and \$140.00 for calendar years 2013 through 2014. *See* §1869(b)(1)(E) of the Act, 74 Fed. Reg. 48976 (Sept. 2, 2009), 75 Fed. Reg. 58407 (Sept. 23, 2010), 76 Fed. Reg. 59138 (Sept. 23, 2011), 77 Fed. Reg. 59619 (Sept. 28, 2012), 78 Fed. Reg. 59702 (Sep. 27, 2013), 42 C.F.R. § 405.1006(b), and 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant’s favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. Section 557 of the Administrative Procedure Act and 70 Fed. Reg. 36386 (June 23, 2005). *De novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into in the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. *See* 42 C.F.R. § 405.1018. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. *See* 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Social Security Act

Medicare Part B provides coverage to eligible beneficiaries for all or part of the cost of “medical and other health services,” a term which is defined by the Act as including, among many other things, durable medical equipment.” *Sections 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Social Security Act; 42 C.F.R. §410.10(h).*

No Medicare payment can be allowed for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member *Section 1862(a)(1)(A) of Title XVIII of the Social Security Act; 42 C.F.R. §411.15(k)(2).*

No payment can be made to the provider or another person unless such information, as may be necessary, has been furnished in support of the medical necessity of the claimed services in order to determine the amount due such provider or other individual. *Section 1833 of Title XVIII of the Social Security Act; 42 C.F.R. §424.5(a)(6).*

When Medicare coverage is precluded under Section 1862(a)(1)(A), i.e., the item was not reasonable and necessary, payment will be made, notwithstanding the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably be expected to know that the item was not covered. This provision is commonly referred to as the limitation of liability provision. *Section 1879 of Title XVIII of the Social Security Act, 42 C.F.R. §411.400.*

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than National Coverage Determinations, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also 42 C.F.R. §405.860.* However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals or local coverage determinations (“LCDs”). 42 C.F.R. § 405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs) or Center for Medicare Services (“CMS”) program guidance when applicable. There is no applicable LCD in the instant case.

Analysis

The amount in controversy is in excess of \$140.00. The QIC issued an unfavorable reconsideration decision on November 8, 2013. By correspondence received on January 8, 2014, the Appellant made a request for an ALJ hearing before OMHA. Therefore, the Appellant’s request was made in a timely manner and the claim satisfies the jurisdictional requirements for an ALJ Hearing before OMHA.

The QIC in its unfavorable decision stated, in part, as follows: "The documentation submitted includes a signed and dated physician order for E1399-RR. However, there were no medical notes submitted for follow up for recurrent glioblastoma that support the need for the item billed. As a result, no payment will be allowed for the item billed as there is insufficient documentation from the patient's medical record to support the medical necessity for a NovoTTF-100A System" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) on May 29, 2013.

The Beneficiary has a medical history that includes recurrent GBM (Ex. 2). He had a gross total resection on February 4, 2010, and subsequently underwent chemotherapy and radiation treatment (*Id.*). He had disease progression found on imaging in February 2011 (*Id.*). He was on bevacizumab from March 2011 until April 2012 (*Id.*). He developed another nodule in the resection bed on December 6, 2012, and was referred to radiation (*Id.*). He had another disease progression in May 2013 (*Id.*). On May 14, 2013, his treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*). The record includes a treatment note from August 20, 2013, which indicates the Beneficiary initiated Novo TTF in May 2013 and that an MRI from August 19, 2013, showed treatment response with overall decreased enhancement (*Id.*). The physician opined the Beneficiary was much improved clinically (*Id.*).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category (*See Ex 2*). Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "*as a factor* in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment.

The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had recurrent GBM and was on his second progression at the time of therapy. He had tried all other FDA approved options for his recurrent GBM. As noted in the clinical record, he had serious side effects from chemotherapy and his previous heart attack was a risk factor to restart bevacizumab. At the time of his therapy, the FDA had approved Optune for his specific condition, and the NCCN Guidelines had recommended this therapy with a level 2B evidence and consensus.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTFT has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. As such, Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the date of service at issue, and the Appellant is entitled to the same.

Conclusions of Law

Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) provided to the Beneficiary on the date of service at issue, and the Appellant is entitled to the same.


Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

AUG 23 2017

Dated:


Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of:	NOVOCURE INC.	OMHA Appeal No.:	1-2431866377
Beneficiary:		Medicare:	Part B
HICN:	*****5064A	Before:	Hon. Roberto M. Gutierrez U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for the Appellant, Novocure Inc.

Procedural History

The Beneficiary, , received miscellaneous durable medical equipment ("DME"), NovoTTF-100A System (E1399) and an INE Insulated Transducer Arrays (E1399) from the Appellant on June 13, 2013, the date of service at issue. The Appellant's claim to Medicare was denied by CGS Administrators, LLC, a Medicare Administrative Contractor ("Contractor"), upon initial and redetermination. On November 18, 2013, C2C Solutions, Inc., a Medicare Qualified Independent Contractor ("QIC"), upheld the prior denials upon reconsideration review. By correspondence received on January 13, 2014, the Appellant made a timely request for an Administrative Law Judge ("ALJ") hearing before the Office of Medicare Hearings and Appeals ("OMHA"). 42 C.F.R. § 405.1014(b)(1).

On July 27, 2017, an ALJ hearing was held by telephone from the OMHA Miami Field Office. The Appellant was represented by Stephanie Hales, J.D. Justin Kelly, RN was present on behalf of the Appellant. All exhibits were admitted into evidence without objection. The attached Exhibit List is incorporated herein by reference. The Appellant's additional evidence was excluded from the record as good cause was not found to admit the new evidence because the evidence was duplicative.

Issues

Whether Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) and INE Insulated Transducer Arrays (E1399) provided to the Beneficiary on the date of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

The amount in controversy is in excess of \$140.00 (Ex. 1). The QIC issued an unfavorable reconsideration decision on November 18, 2013 (*Id.*). By correspondence received on January 13, 2014, the Appellant made a request for an ALJ hearing before OMHA (Ex. 3).

The QIC in its unfavorable decision stated, in part, as follows: "The documentation on record does not substantiate the items at issue fall within a benefit category. Additionally, the record does not contain proof of delivery indicating the beneficiary received the items at issue. As such, the record has not satisfied all requirements for the items at issue according to Medicare policy" (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) and an INE Insulated Transducer Arrays billed under miscellaneous durable medical equipment (E1399) on June 13, 2013.

The Beneficiary has a medical history that includes gliomastosis cerebri (Ex. 2). She underwent chemotherapy and radiation treatment (*Id.*). On May 30, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*).

The Food and Drug Administration ("FDA") approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population (*Id.*). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009 (*Id.*). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life (*Id.*).

The record includes a publication from the National Comprehensive Cancer Network ("NCCN") Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," which reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM (*Id.*). Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment (*Id.*).

At the hearing, the Appellant's representative testified that Optune (which was previously known as the NovoTTF-100A system) is a portable, wearable device that delivers tumor treating fields,

which are alternating electric fields, to the brain. The device consists of a portable, electric field generator connected to a portable battery that is connected to 4 insulated transducer arrays that are placed on the patient's scalp. The device generates electric currents that go through the transducer arrays, which creates the tumor treating fields. In 2013, after receiving billing rights from CMS, the Appellant billed the device under 2 components: (1) the electric field generator, billed under E1399; and (2) the insulated transducer arrays, billed as a DME supply under miscellaneous code A9900. In 2014, effective January 1, 2014, CMS issued two HCPCS codes for the NovoTTF-100A system: E0766 for the device; and A4555 for the transducer arrays. At that time, CMS designated the therapy as DME requiring frequent and substantial servicing.

The therapy delivers alternating electric fields to the brain. The electric fields disrupt the formation of the mitotic spindle in the dividing cancer cell. The therapy is similar to taxing chemotherapy insofar as it inhibits the formation of the mitotic spindle, which leads to program cell death. The therapy does not affect non-dividing cells and is frequency-tuned specifically to GBM cells.

The therapy was approved by the FDA in 2011 under the pre-market approval pathway, which is the most stringent device approval pathway. Only 2% of medical devices are approved through this pathway. That approval was based on a randomized controlled trial in recurrent GBM of 243 patients that compared using Optune by itself to physician-choice chemotherapy. The FDA concluded in its initial approval that the NovoTTF-100A system treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness, and a better quality of life compared to chemotherapy in the control arm of the study. This trial was published in the *European Journal of Cancer* in 2012, which is a CMS-recognized medical journal. According to the Appellant, Optune is included in the NCCN Guidelines with a consensus 2B recommendation for recurrent GBM and a 2A uniform consensus recommendation for newly diagnosed GBM in combination with temozolomide.

The Appellant argued that the clinical data in the NCCN Guideline inclusions are sufficient for coverage. The Appellant pointed out that a majority of insurance companies provide coverage for this therapy for the most appropriate patients due to the broad medical consensus supporting its use and effectiveness in patients like the Beneficiary. The therapy was established and proven as an option for recurrent GBM through peer reviewed journals, clinical guidelines and is widely recognized in the field nationwide. GBM is an aggressive, primary brain cancer. Prior to Optune being FDA approved, patients had a life expectancy with treatment of about 12 to 15 months. A disease is labeled recurrent after a patient has progressed after initial therapy. A 1 year survival rate for a recurrent GBM patient is about 10%. When GBM recurs, about 20% of patients are eligible for a reoperation or an additional resection. Most patients are not eligible for additional radiation because they have already maxed out their radiation dose with the initial treatment. A chemotherapy regimen that has already been tried and failed is not an option when a tumor recurs or progresses post-treatment. As a result, recurrent GBM patients have very limited treatment options.

The Appellant's representative further testified that the Beneficiary was diagnosed with a right sided GBM in April 2013. She underwent a CT guided biopsy, confirming glioblastoma. She subsequently received intensity-modulated radiation therapy ("IMRT") and temozolomide. She experienced a recurrence in her tumor, and due to the extensiveness of her disease, her physician prescribed Optune, which she began on June 13, 2013. She had recurrent GBM at the time of

therapy. Her physician believed this was the best treatment option for her given the extensiveness in her disease as documented in the medical record. At the time of therapy, Optune was FDA-approved for her specific condition, and the clinical guidelines from the NCCN recognized this option for this indication, with a category 2B level of evidence and consensus.

The Appellant's representative also argued that the published literature reflects the clearly documented effectiveness of the device, and the medical records show the reasonableness and necessity specifically for this beneficiary for this device at the time it was prescribed by her physician, consistent with the FDA labeling under the rigorous pre-market approval process. The Appellant's representative indicated the reconsideration decision notes that NCD 280.1 describes limitations regarding DME. The Appellant argued that the DME reference list in the NCD is a non-exhaustive list of covered DME, and the NCD specifically specifies that when the DME MAC receives a claim for an item of equipment that does not appear to fall in any generic category, the MAC has authority and responsibility to determine whether those items are covered under the DME benefit. The Appellant further argued that because the NovoTTF-100A system is not in that list, it is appropriate for the MAC in these cases to make an individualized determination of the item and whether it meets the DME benefit category. The Appellant contends that under that analysis, the NovoTTF-100A system is appropriately categorized as DME and that the single use insulated transducer arrays are appropriately categorized as supplies necessary for the effective use of that DME. The Appellant's representative pointed out that Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category. Therefore, the MAC was mistaken in its determination.

Principles of Law

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges ("ALJ's") within OMHA issue binding decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.*

For requests filed in calendar years 2010 through 2012, the minimum amount remaining in controversy required for an ALJ hearing is \$130.00 (following application of any co-insurance or deductible) and \$140.00 for calendar years 2013 through 2014. *See* §1869(b)(1)(E) of the Act, 74 Fed. Reg. 48976 (Sept. 2, 2009), 75 Fed. Reg. 58407 (Sept. 23, 2010), 76 Fed. Reg. 59138 (Sept. 23, 2011), 77 Fed. Reg. 59619 (Sept. 28, 2012), 78 Fed. Reg. 59702 (Sept. 27, 2013), 42 C.F.R. § 405.1006(b), and 42 C.F.R. § 405.1006(d)(1)(ii).

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. Section 557 of the Administrative Procedure Act and 70 Fed. Reg. 36386 (June 23, 2005). *De novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. *See* 42 C.F.R. § 405.1018. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. *See* 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Social Security Act

Medicare Part B provides coverage to eligible beneficiaries for all or part of the cost of "medical and other health services," a term which is defined by the Act as including, among many other things, durable medical equipment." *Sections 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Social Security Act; 42 C.F.R. §410.10(h).*

No Medicare payment can be allowed for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member *Section 1862(a)(1)(A) of Title XVIII of the Social Security Act; 42 C.F.R. §411.15(k)(2).*

No payment can be made to the provider or another person unless such information, as may be necessary, has been furnished in support of the medical necessity of the claimed services in order to determine the amount due such provider or other individual. *Section 1833 of Title XVIII of the Social Security Act; 42 C.F.R. §424.5(a)(6).*

When Medicare coverage is precluded under Section 1862(a)(1)(A), i.e., the item was not reasonable and necessary, payment will be made, notwithstanding the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably be expected to know that the item was not covered. This provision is commonly referred to as the limitation of liability provision. *Section 1879 of Title XVIII of the Social Security Act, 42 C.F.R. §411.400.*

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than National Coverage Determinations, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also 42 C.F.R. §405.860.* However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals or local coverage determinations (“LCDs”). 42 C.F.R. § 405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs) or Center for Medicare Services (“CMS”) program guidance when applicable. There is no applicable LCD in the instant case.

Analysis

The amount in controversy is in excess of \$140.00. The QIC issued an unfavorable reconsideration decision on November 18, 2013. By correspondence received on January 13, 2014, the Appellant made a request for an ALJ hearing before OMHA. Therefore, the Appellant’s request was made in a timely manner and the claim satisfies the jurisdictional requirements for an ALJ Hearing before OMHA.

The QIC in its unfavorable decision stated, in part, as follows: “The documentation on record does not substantiate the items at issue fall within a benefit category. Additionally, the record does not contain proof of delivery indicating the beneficiary received the items at issue. As such, the record has not satisfied all requirements for the items at issue according to Medicare policy” (Ex. 1).

The Beneficiary received from the Appellant a NovoTTF-100A System billed under miscellaneous durable medical equipment (E1399) and an INE Insulated Transducer Arrays billed under miscellaneous durable medical equipment (E1399) on June 13, 2013.

The Beneficiary has a medical history that includes gliomastosis cerebri (Ex. 2). She underwent chemotherapy and radiation treatment (*Id.*). On May 30, 2013, her treating physician prescribed the NovoTTF-100A System, which furnishes TTFT (*Id.*).

The FDA approved the manufacturer's premarket approval application for the NovoTTF-100A System in 2011 (*Id.*). The device, which furnishes TTFT, is indicated for treatment of adult patients with histologically-confirmed GBM, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy (*Id.*).

As an initial matter, the undersigned finds that the NovoTTF-100A is an item of DME. Medicare regulations define DME as equipment that can withstand repeated use; is primarily and customarily used to serve a medical purpose; generally is not useful to an individual in the absence of an illness or injury; and is appropriate for use in the home. 42 C.F.R. § 414.202. It is apparent from the record that the NovoTTF-100A system can withstand repeated use, is primarily used for a medical purpose, would not likely be useful to a beneficiary in the absence of an illness or injury, and is appropriate for use in a beneficiary's home. Moreover, as the Appellant's representative pointed out, Novocure requested and received a review by CMS of the benefit category in 2013, and a letter from Joel Kaiser at CMS's Division of DMEPOS Policy dated July 26, 2013, notes that CMS believes the NovoTTF-100A system falls within the DME benefit category (*See Ex 2*). Therefore, the NovoTTF-100A system is an item of DME. However, a finding that the NovoTTF-100A system is an item of DME does not compel a conclusion that the device is covered by Medicare.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110.

The regulations state that "CMS *may consider* for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "*as a factor* in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for recurrent GBM. Nevertheless, the undersigned finds that the evidence, as summarized below, establishes that, at the time the device was furnished, the NovoTTF-100A system had gained general acceptance within the medical community in the treatment of recurrent GBM and thus, meets medical necessity standards for Medicare coverage.

The record supports the NovoTTF-100A system is not experimental and investigational. There is evidence in the record that establishes that TTFT has gained general acceptance within the medical community as a safe and effective treatment option for patients with recurrent GBM. The Appellant submitted a letter of medical necessity from the Beneficiary's treating physician, indicating the NovoTTF-100A system is the only chronic treatment for recurrent GBM that has been studied in a randomized controlled trial and has demonstrated a survival time benefit in this population. In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (i.e., surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until May 2009. The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy but with fewer side-effects and an improved quality of life. Moreover, a publication from the NCCN Clinical Practice Guidelines in Oncology entitled, "Central Nervous System Cancers," reflects that as of the date of the publication, December 21, 2012, alternating electric field therapy was considered an effective treatment option for recurrent GBM. Along with palliative supportive care, chemotherapy, surgery/reirradiation, it is considered a fourth modality of cancer treatment.

The evidence of record also reflects the NovoTTF-100A system was medically reasonable and necessary for this beneficiary. The Beneficiary had recurrent GBM at the time of therapy. Her physician believed this was the best treatment option for her given the extensiveness in her disease as documented in the medical record. At the time of therapy, Optune was FDA-approved for her specific condition, and the clinical guidelines from the NCCN recognized this option for this indication, with a category 2B level of evidence and consensus.

Therefore, at the time the device was furnished to the Beneficiary, the NovoTTF-100A System was reasonable and necessary and, therefore, is covered under Section 1862(a)(7) of the Social Security Act. The record supports the efficacy of the NovoTTF-100A system in treating recurrent GBM and that TTFT has gained general acceptance within the medical community as a modality of cancer treatment for patients with recurrent GBM. Since the NovoTTF-100A System at issue is medically reasonable and necessary, the INE insulated transducer arrays is also covered under Section 1862(a)(7) of the Social Security Act. As such, Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) and INE Insulated Transducer Arrays (E1399) provided to the Beneficiary on the date of service at issue, and the Appellant is entitled to the same.

Conclusions of Law

Medicare coverage exists for the miscellaneous durable medical equipment, NovoTTF-100A System (E1399) and INE Insulated Transducer Arrays (E1399) provided to the Beneficiary on the date of service at issue, and the Appellant is entitled to the same.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED

Dated:

AUG 23 2017



Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



**Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami Field Office
Miami, FL**

Appeal of: Beneficiary: HICN: *****1590A	ALJ Appeal No.: 1-3087132105 Medicare: Part C Before: Hon. Roberto M. Gutierrez U.S. Administrative Law Judge
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SUMMARY OF DECISION

After carefully considering the evidence and arguments presented in the record the undersigned Administrative Law Judge (ALJ), enters this **FULLY FAVORABLE DECISION** for The Beneficiary is the Appellant in this case.

PROCEDURAL HISTORY

Dissatisfied with the unfavorable reviews by the Medicare Advantage Part C Plan, Blue-Cross/Blue Shield (BlueMedicare HMO) and by the Qualified Independent Contractor (QIC), Appellant filed this timely appeal for a review of the denial of pre-approval for payment of Tumor Treatment Field Therapy (TTFT)

On January 6, 2015, the Office of Medicare Hearings and Appeals received Appellant's timely request for a hearing before an Administrative Law Judge. In cases like the one at hand, where the basis of an appeal is a Medicare Advantage Plan's refusal to provide services, the projected value of those services is used to calculate the amount remaining in controversy. 42 C.F.R. § 422.600(c). The undersigned finds that in this case, the amount in controversy meets the jurisdictional requirements for review by an ALJ at the hearing level. Accordingly, this claim is properly before the undersigned for adjudication having met all jurisdictional predicates.

After proper notice to all pertinent parties, the undersigned held a telephone hearing on June 3, 2015. Rosie Asikis, Team Leader for Novucare appeared at the hearing as the Beneficiary's representative and the Beneficiary, **REDACTED** were present at the hearing. Also present at the hearing on behalf of the Medicare Part C Plan, BCBS of North Carolina were Wendy Kiger, Appeals Specialist, Andy Bonin, M. D., Medical Director and Beth McConnell, R.N., Manager of Appeals. The record consists of Exhibits 1 through 6 which the undersigned entered into the evidence at the hearing without any objections by the parties.

ISSUES

The issue before the ALJ is whether the Part C health care plan is obligated to cover and pay a

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non-participating provider for the NovoTTF-100A System, HCPCS/CPT E0766, used for Tumor Treatment Field Therapy for glioblastoma under the provisions of Medicare Part C?

FINDINGS OF FACT

After careful consideration of the entire record, including the hearing testimony, the undersigned ALJ makes the following findings of facts as set forth by preponderance of the evidence. This case concerns a request for Part C coverage of a medical device from a non-participating DME provider, who is requesting in-network exception to the Medicare Part C coverage for an item which is not considered medically reasonable and necessary by the local Medicare Administrative Contractor's LCD.

The Beneficiary, a _____, has recent onset of Glioblastoma (GBM), an "orphan disease" with limited available treatment options. First onset of symptoms occurred in October 2014, when the Beneficiary presented with multiple small seizures. The Beneficiary subsequently developed right arm and leg sensory complaints and motor function deficits. An MRI from November 2014 revealed a parafalcine lesion and Appellant underwent a bilateral frontal parietal craniotomy with resection. The biopsy report revealed Grade IV GBM for which she was started simultaneously on chemo and radiation therapy on December 29, 2014, with poor response. Based on the Beneficiary's response to treatment and continued symptoms, the treating oncologist recommended Novo TTFT as the best option for treating the beneficiary's glioblastoma tumor.

The well documented record includes medical literature, medical journals, articles from clinical trials, documentation by the Food and Drug Administration (FDA) regarding the device, as well as the treating physician medical statement explaining the patient's clinical picture and the rationale for using NovoTTF in the Beneficiary's case (Ex. 3). According to these records, the Novo TTF-100A System is an innovative approach to cancer treatment which uses tumor treating fields (TTF) to interfere with the division of malignant (cancerous) cells. TTF therapy is a locally (or regionally) delivered treatment. It uses electric fields within the human body that are inferred to disrupt the rapid cell division exhibited by cancer cells. GBM patients treated with TTFT wear insulated transdural arrays on the scalp attached to a portable electric field generator. The system then uses electric field to disrupt the multiplication of tumor cells and to destroy them.

Ms. Asikis' testimony and the evidence of record show the FDA had approved this item for the treatment of Glioblastoma in April 2011, as safe and effective. She requested that the treatment be approved at in network level as there are no other providers of this service in the Plan's network. Thus, she asked for an in-network exception. Ms. Asikis argued that this treatment has been covered and approved commercially by other insurers, including other patients served by Blue-Cross/Blue Shield of North Carolina. Ms. Asikis further explained that the issue with the categorical denial of the device in the LCD had to do with the fact that FDA had previously fast-tracked approval for the item at issue as a bone stimulator, which is not what this treatment is. Ms. Asikis also noted that the MAC was working on changes to the LCD due to these issues. Ms. Asikis explained that the Beneficiary had been diagnosed with GBM and had exhausted all treatment modalities available (surgery, chemo and radiotherapy). In this case, the medical and testimonial evidence, including the patient's statements, indicate she continues to have problems with balance and has fallen several times despite surgical, chemotherapy and radiation treatment.

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The Novo TTF-100A System received FDA approval in April 2011 based on trials of a large randomized controlled trial of patients with recurrent GBM which showed treatment with the system had minimal toxicity which allowed for long-term treatment with the device (Ex. 3, pp. 34-38). TTFields as a single modality demonstrated a higher response rate and longer time to treatment failure compared to the current best available chemotherapy treatment. On June 30, 2014, CMS rescinded the DMEPOS fee schedule payment amount of the E0766, the code for the NovoTTF-100A System, retroactive to January 1, 2014 and designated as a Durable Medical Equipment paid on a rental basis with supplies, not subject to capped rental or purchase requirements. CMS payment will be done on a case-by-case basis based on the carrier pricing, which does not guarantee payment of the claim, therefore there is evidence that CMS will consider some coverage of claims for this device.

In terms of the applicability of the new technology to newly diagnosed patients, as the Beneficiary in this case, data from clinical trial EF-14 randomized controlled trial in newly diagnosed patients demonstrated superior efficacy both in progression free survival as well as in overall survival. The rate of success was so compelling that the independent data monitoring committee recommended the trial be terminated so that patients undergoing the standard of care arm could cross over and be treated with the TTFT device (Ex. 3, p. 31). These results were first made public at the Society of Neuro-Oncology Annual Meeting in November 2014. The FDA approved the crossover of the patients on the control arm to the TTFields arm on December 1, 2014.

Dr. Bonin acknowledged during the hearing that BCBS had previously provided coverage of the device and agreed that the language of the LCD was conclusory and not clear on the basis and rationale for the HCPCS/CPT being considered not medically reasonable and necessary. Dr. Bonin also explained that the BCBS had allowed payment at a previous time as an exception because there were no other in-network providers. However, after the LCD was issued, the Plan was no longer able to provide an exception as it was bound to follow the LCD.

The QIC's reconsideration review and rationale for the denial did not provide any explanation regarding the categorical denial of the device being used for tumor treatment field therapy (E0766).

LEGAL FRAMEWORK

The Medicare Program is the federal health insurance program for people 65 and older and certain disabled people and is governed by the provisions set forth in Title XVII of the Social Security Act (42 U.S.C. § 1395 et seq.). Medicare is divided into several parts, among them Part C (Medicare Advantage Plans). Advantage plans are expected to stay apprised of new and/or changing Medicare Part A and Part B coverage policies, including those that result from CMS's National Coverage Determination (NCD) process and any other processes and information dissemination sent to providers.

If an individual is dissatisfied with the reconsideration of an initial determination he or she is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided the individual filed a timely request for hearing and the case, in this instant,

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Part C claim meets (or potentially meets) the amount in controversy requirements to be entitled to a hearing before an ALJ (42 C.F.R. § 405.1014 and the Act, Title V, § 1869(b)(1)(A)).

The Secretary delegated her authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA (*See* 70 Fed. Reg. 36386, 36387 (June 23, 2005)). The Administrative Law Judges ("ALJs") within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.* The standard of review at the Administrative Law Judge hearing level is "*de novo*" since an ALJ is required to consider anew the facts and the law at hand (70 Fed. Reg. 36386 (June 23, 2005); *see also In re Atlantic Anesthesia Associates, P.C.*, MAC (June 2004) ("An ALJ qualified and appointed pursuant to the Administrative Procedure Act acts as an independent finder of fact in conducting a hearing pursuant to §1869 of the Act. This requires *de novo* consideration of the facts and law.

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing (42 §CFR 405.1000, *et seq.* and § 405.1032(a)).

APPLICABLE STATUTES AND REGULATIONS

Medicare Part C, Medicare+Choice Program is covered under Section 1851 *et seq.* of the Social Security Act [42 U.S.C. 1395w-21] of the Social Security Act. Under these provisions, eligible individuals are entitled to elect to receive benefits (other than qualified prescription drug benefits) under the title either through the original Medicare fee-for-service program under parts A and B, or through enrollment in a Medicare+Choice plan under this part. Each Medicare+Choice plan shall provide to members enrolled under this part, through providers and other persons that meet the applicable requirements of this title and part A of title XI, benefits under the original Medicare fee-for-service program option (and, for plan years before 2006 and additional benefits required under section 1854(f)(1)(A)).

In the case of a Medicare+Choice organization that offers a Medicare+Choice plan in an area in which more than one local coverage determination is applied with respect to different parts of the area, the organization may elect to have the local coverage determination for the part of the area that is most beneficial to Medicare+Choice enrollees (as identified by the Secretary) apply with respect to all Medicare+Choice enrollees enrolled in the plan and may elect qualified prescription drug coverage in accordance with section 1860D-1. The Statute requires that the plans provide full disclosure of all the Benefits of the plan on a yearly basis. The statute also requires the plans to provide methods of redress or exceptions where applicable or warranted. Part C defines "basic benefits" as "all Medicare covered services, except hospice services." Mandatory supplemental benefits are defined as "services not covered by Medicare that an MA enrollee must purchase as part of an MA plan that are paid for in full, directly by (or on behalf of) Medicare enrollees, in the form of premiums or cost sharing.

Durable Medical Equipment is covered by Section 1861(n) (42 U.S.C. [42 U.S.C. 1395x]). The term "durable medical equipment" includes iron lungs, oxygen tents, hospital beds that are to be used on the patient's home, whether furnished on a rental basis or purchased; except that this term does not include any equipment furnished by a supplier who has used, for the demonstration

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and use of specific equipment, an individual who has not met such minimum training standards as the Secretary may establish with respect to the demonstration and use of such specific equipment.

Section 1862(a)[42 U.S.C. 1395y] provides the grounds for exclusions from coverage and states that notwithstanding any other provision of this title, Medicare Part A or B will not pay for items or services which are not medically reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

The Medicare Advantage (MA) program (Part C of the Act) provides that an MA organization offering an MA plan must provide enrollees, at a minimum, with all basic Medicare-covered services by furnishing the benefits directly or through arrangements, or by paying for approved benefits (42 C.F.R. §422.101). These services include basic benefits, as well as mandatory and optional supplemental benefits, among others.

The applicable Medicare statutes, rules and regulations state that Medicare will cover an item if the item is: eligible for a defined Medicare benefit category; reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and meets all other applicable Medicare statutory and regulatory requirements. For the items addressed in this local coverage determination, the criteria for "reasonable and necessary", based on Social Security Act § 1862(a) (1) (A) provisions, are defined by the following indications and limitations of coverage and/or medical necessity.

Title XVIII, Section §1871 ([42 U.S.C. 1395hh]), *Regulations*, authorizes the Secretary to prescribe such regulations as may be necessary to carry out the administration of the insurance programs under this title. When used in this title, the term "regulations" means, unless the context otherwise requires, regulations prescribed by the Secretary. Section 1871(a)(2) states that other than national coverage determinations no rule, requirement, or other statement of policy () that establishes or changes a substantive legal standard governing the scope of benefits, the payment for services, or the eligibility of individuals, entities, or organizations to furnish or receive services or benefits under this title shall take effect unless it is promulgated by the Secretary by regulation (*See also* 42 C.F.R. §405.860). Under these provisions national coverage decisions (*hereinafter* NCDs) are binding upon Administrative Law Judges.

The Benefits Improvement and Protection Act of 2000 (BIPA 2000) process converted all Local Medical Review Policies (LMRPs) to LCDs. The difference between LCDs and previously written LMRPs is that LCDs contain only reasonable and necessary conditions of coverage as allowed under section 1862(a)(1)(A) of the Act. Local coverage determinations (LCDs) are defined in Section 1869(f)(2)(B) of the Social Security Act (the Act). The provisions of this section state that the term 'local coverage determination' means a determination by a fiscal intermediary or a carrier under part A or part B, as applicable, respecting whether or not a particular item or service is covered on an intermediary- or carrier-wide basis under such parts, in accordance with section 1862(a)(1)(A)." Administrative Law Judges are not bound by LCDs, LMRPs or CMS program guidance (such as program memoranda and manual instructions), but must give substantial deference to these policies. If an ALJ declines to follow a policy in a particular case, the ALJ or MAC decision must explain the reasons why the policy was not followed and this decision to depart from these policies will apply only to the specific claim and will not have precedential effect on future claims.

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Notwithstanding any other provision of Title XVIII of the Act, Section 1862(a) of the Act [42 U.S.C. § 1395y(a)(1)(A)] limits the payments that may be made under Part A or Part B, stating in pertinent part that, "no payment may be made under Part A or Part B for any expenses incurred for items or services — (1)(A) which . . . are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member . . ." *Id.*; See also 42 C.F.R. § 411.15(k)(1.) Additionally, § 1833(e) of the Act [42 U.S.C. § 1395l(e)] prohibits Medicare payment for any claim that lacks such information as may be necessary in order to determine the amounts due such provider.

POLICY & GUIDANCE

In general, for Medicare to cover and pay for any item or services, the item or service must: 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements. For the items addressed in this local coverage determination, the criteria for "reasonable and necessary", based on Social Security Act § 1862(a)(1)(A) provisions.

CMS Medicare Managed Care Manual, Publication 100-16, contains policy guidance regarding Medicare Part C plans and provides that An MA organization (MAO) offering an MA plan must provide enrollees in that plan with all Part A and Part B original Medicare services, if the enrollee is entitled to benefits under both parts, and Part B services if the enrollee is a grandfathered "Part B only" enrollee. The MAO fulfills its obligation of providing original Medicare benefits by furnishing the benefits directly, through arrangements, or by paying on behalf of enrollees for the benefits. Basic benefits must be furnished through providers meeting requirements that are specified in 42 CFR § 422.204(b)(3). Accordingly, items or services classified as an original Medicare benefit must be covered by every MA plan if:

- Its coverage is consistent with general coverage guidelines included in original Medicare regulations, manuals and instructions (unless superseded by written CMS instructions or regulations regarding Part C of the Medicare program);
- It is covered by CMS' national coverage determinations (see Sections 90.3 and 90.4, below); or
- It is covered by written coverage decisions of local Medicare Administrative Contractors (MACs) with jurisdiction for claims in the geographic area in which services are covered under the MA plan, as described in Section 90.2 below.

In the attendant case, the applicable provisions regarding applicability of LCDs to items and devices are contained in Chapter 4, Benefits and Beneficiary Protections, Section 90. In general, Medicare Part C plans must cover all benefits that would be covered under Medicare Parts A and B, included those items which are medically reasonable and necessary and used to diagnose and treat complications arising from participating in qualifying clinical trials. Medicare Clinical Trial policies apply.

The policy does not withdraw Medicare coverage for items and services that may be covered according to Local Coverage Determinations (LCDs) or the regulations on category B investigational device exemptions found in 42 CFR 405, Subpart B, 411.15, and 411.406. MA

plans are to use LCDs for guidance, but are still bound to use other Medicare applicable statutes, rules and regulations in interpreting the LCDs or advising the applicability of a specific LCD to an item, including deviating from a specific LCD if warranted by the Medicare record and if other Medicare regulations may apply in one case. The only time a plan is bound to use an LCD is in those cases in which **one Medicare A/B MAC processes all of the claims for a particular Medicare-covered item or service for all Medicare beneficiaries around the country**. This generally occurs when there is only one provider of a particular item or service (for example, certain pathology and lab tests furnished by independent laboratories) and a single MAC handles all the claims for this provider. *In this situation, MA plans must follow the coverage policy reflected in an LCD issued by the A/B MAC that enrolled the provider and processes all of the Medicare claims for that item or service.* Of note in this case is that in November 2014, BlueCross BlueShield of North Carolina issued a Corporate Medical Policy which declared "Tumor Treatment Fields Therapy for Glioblastoma" as investigational for all applications, therefore not covered because BCBSNC did not provide coverage for investigational services or procedures (See https://www.bcbsnc.com/.../tumor-treatment-fields_therapy_for_glioblastoma.pdf, last viewed June 8, 2015).

The attendant local coverage determination, LCD L34665 (L34823) HCPCS/CPT E0766 Electrical Stimulation Device Used for Cancer Treatment, and Policy Article A152667, provide the following indications and limitations of coverage and/or medical necessity. The LCD states that Tumor Treatment Field Therapy (E0766) will be denied as not reasonable and necessary. Whereas the LCD categorically denies the item as not medically reasonable and necessary, the Policy Article states that tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act §1861(s)(6)). The Article specifies that in order for an equipment to be eligible for reimbursement, it must meet the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination and any other specific statutory payment policy requirements. The Article explains that Code E0766 is in the frequent and substantial service payment category, usually reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories. Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers. This HCPCS/CPT Code was submitted by the manufacturer for an HCPCS code verification review and included in the Medicare Pricing, Data Analysis and Coding database since January 1, 2014, which implies that there might coverage grounds for the item or device, but does not guarantee payment by Medicare as these claims are usually decided on a case-by-case basis.

Medicare Part C Plan: Evidence of Coverage Plan for BCBS North Carolina

The EOC defines Medicare-Covered Services, as those services that are covered by Medicare Part A and Part B. Chapter 12 explains that all Medicare health plans, including this Plan C must cover all services that are covered by Medicare Part B.

Chapter 4, Medical Benefits Chart, indicates that the Plan covers durable medical equipment and related supplies that are covered by the original Medicare, requiring only that the Beneficiary seek prior approval for DMEs with a purchase price greater than \$600.00.

Chapter 12 of the EOC, *Definition of Important Words*, defines "Durable Medical Equipment"

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as "certain" medical equipment that is ordered by the Beneficiary's physician for medical reasons, and sets forth as examples walkers, wheelchairs, or hospital beds. Chapter 12 also defines "Evidence of Coverage (EOC) and Disclosure Information" as the actual document along with the enrollment for and any other attachments, riders, or other optional coverage selected, which explains coverage, the Plan's obligations and the member's rights under the plan (Ex. 1, p. 217).

The EOC does not contain language indicating that it is bound by a local coverage determination, but it does state that it must and will follow Medicare "original" benefits to all plan members.

Analysis

As a matter of law, the LCD is conclusory because it denies coverage of Tumor-Treatment Field Therapy for GBM as not medically reasonable and necessary without providing any rationale supporting the policy. In specific, the LCD does not classify the DME as investigational in nature, or as being not safe and effective, nor does it provide any other information as to whether the item or device is subject to one of the exclusions noted elsewhere in the Act.

The physician for the plan acknowledged that the LCD is conclusory but argues that the Plan is bound by the LCD.

Of note in this case is the fact that in November 2014, Corporate BCBS in North Carolina issued a Policy decision not to pay for TTFT E0766 because it was investigational in nature. Dr. Bonin testified that the claim was denied based on an LCD which he has already admitted is conclusory, but acknowledges that the medical evidence shows the item at issue was medically reasonable and necessary based on the diagnosis and on the fact that the Beneficiary has tried and exhausted all chemotherapy and radiation therapy, in addition to surgical treatment.

The provider, a non-participating DME provider, has requested an in-network exception to the plan for coverage and has presented documentation supporting this exception. The same Part C Plan has previously reimbursed a claim for the same item/service, but now declines to reimburse based on an LCD which the medical expert for the Plan acknowledges is conclusory and lacks supporting rationale.

It is based on the above that the undersigned ALJ issues this **FULLY FAVORABLE DECISION**. The item is covered and payable by Medicare because the Beneficiary has GBM, has undergone and exhausted all other forms of treatment, including surgical, chemotherapy and radiation treatment. None of these have helped the Beneficiary. The provider is entitled to the in-network exception to the plan for coverage and reimbursement, as there are no other DME providers in the network that currently provide this DME.

Conclusion of Law

The plan is to cover and pay for HCPCS/CPT E0766 as medically reasonable and necessary and covered under Medicare statutes, rules and regulations.

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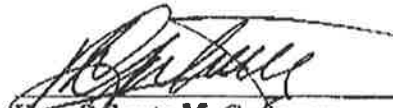
Order

The Medicare contractor is **DIRECTED** to process this claim in accordance with this decision.

JUN 19 2015

Dated: JUN 19 2015

SO ORDERED,


Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida

Appeal of:	REDACTED	OMHA Appeal No.: 1-8007682782
Beneficiary:		Medicare: Part B
Medicare No.:		Before: Hon. Roberto M. Gutierrez U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record, a **FAVORABLE** decision is entered for REDACTED ("Appellant-Beneficiary").

Procedural History

The Appellant-Beneficiary received an electrical stimulation device, NovoTTF-100A System (E0766) from December 30, 2017 to February 28, 2018. (Exh. 1). The Medicare Administrative Contractor ("Contractor") denied the claims upon initial determination and redetermination. (*Id.*). On August 14, 2018, the Medicare Qualified Independent Contractor ("QIC") upheld the prior denials upon reconsideration review. (*Id.*). By correspondence received on October 15, 2018, Appellant-Beneficiary made a timely request for an Administrative Law Judge ("ALJ") hearing before the Office of Medicare Hearings and Appeals ("OMHA"). 42 C.F.R. § 405.1014(b)(1). The amount in controversy exceeds the jurisdictional threshold for a hearing defined in § 1869(E) of the Social Security Act. A telephonic hearing was held on November 26, 2018. Debra Parrish, J.D., and Julie Miles, R.N., appeared in behalf of Appellant-Beneficiary. The witness testified under oath. During the hearing, Exhibits 1 to 5 were admitted into evidence without objection.

Issues

Whether Medicare coverage exists for the electrical stimulation device, NovoTTF-100A System (E0766) provided to the Appellant-Beneficiary on the dates of service at issue, and, if not, who is responsible for the non-covered charges?

Findings of Fact

Appellant-Beneficiary, a 78-year-old-male, received an electrical stimulation device, NovoTTF-100A System (E0766) from December 30, 2017 to February 28, 2018. Optune, previously known as the NovoTTF-100A System, is a durable medical equipment that delivers alternating electric fields or tumor treating fields to the brain. (Exh. 4, p. 10). The device consists of an electric field generator which is connected to four insulated transducer arrays. (*Id.*). The arrays are placed on the patient's scalp and deliver the tumor treating fields therapy (TTF therapy) to the glioblastoma. (*Id.*). The fields slow the replication of the cancer cells or stop their growth altogether. (*Id.*). The fields may also destroy some of the cancer cells. (*Id.*). Optune is FDA-approved for recurrent and newly diagnosed GBM brain tumors. (*Id.*). Optune is a portable battery or power supply operated device, which may be carried by the patients in an over-the-shoulder bag or backpack and receive continuous treatment without changing their daily routine. (Exh. 2, p. 47). It is a portable, wearable medical device, and patients maintain normal daily activities while receiving TTF therapy continuously. (*Id.* at 80).

On January 1, 2014, CMS classified the Optune device as a DME requiring frequent and substantial servicing, which is billed under HCPCS code E0766, as a monthly rental through the duration of medical necessity. (Exh. 4, p. 11). The Optune System was the subject of numerous peer-reviewed published studies that demonstrate the safety and efficacy of the Optune System and TTF therapy generally. (*Id.* at 11). The studies are reported in some of the most prestigious journals in the country including the Journal of the American Medical Association. (*Id.*). Optune is included in the National Comprehensive Cancer Network (NCCN) guidelines for recurrent glioblastoma and for newly diagnosed GBM in combination with temozolomide. (*Id.*). In particular, for newly diagnosed glioblastoma, the NCCN guidelines (considered the gold standard for oncology management) give a level one recommendation for TTF therapy, i.e., a consensus exists among the experts based on the highest levels of evidence, that the treatment is recommended. (*Id.*). The Data Safety Monitoring Board for the clinical trial for the newly diagnosed glioblastoma (and patients that suffered recurrences during the trial) found the data so compelling, that they recommended early termination and allowing patients who were not receiving the treatment to be able to cross over and receive the treatment, deeming it unethical to withhold it, and the FDA agreed. (*Id.* at 12). It has widespread adoption and virtually every major payor in the United States covers the Optune System for individuals diagnosed with a glioblastoma. (*Id.* at 12). These payors include Highmark, Aetna, Anthem, Humana, Kaiser, UnitedHealthcare, Cigna, Harvard Pilgrim, Geisinger, HealthPartners, and several Blue Cross plans. (*Id.*). The Food and Drug Administration ("FDA") approved the NovoTT-100A system, under the pre-market approval (PMA) pathway in April 2011 (Exh. 2, pp. 80, 96). The PMA approval pathway is the most rigorous medical device approval pathway and is analogous to the FDA new drug application (NDA) pathway. (*Id.*). The FDA approved the device on the basis of results from a multi-center randomized controlled pivotal (phase III) trial. (*Id.*). The FDA PMA approval followed a positive vote from the FDA's Independent Medical Device Advisory Committee's Neurological Devices Panel. (*Id.*). The NovoTTF-100A is intended as a treatment for adult patients with histologically-confirmed GBM, following histologically or radiologically-confirmed recurrence in the supra-tentorial region of the brain after receiving chemotherapy (*Id.*). In the EF-11 study, 237 patients with previously diagnosed GBM who had relapsed or progressed despite conventional therapy (surgery and chemo-radiotherapy followed by chemotherapy) received TTFT using the NovoTTF-100A system from September 2006 until

May 2009. (*Id.* at 96). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy, but with fewer side-effects, including a reduced hospitalization rate and provides the patients with an improved quality of life (*Id.* at 111). Patients receiving chemotherapies suffer from wound healing complications, infections, diarrhea, constipation, nausea, vomiting, pain, decreased blood cell counts and their complications, bleeding disorders and thromboembolic events (e.g. stroke). (*Id.* at 90). The manufacturer has applied the CE Mark to the device and received marketing approvals in the UK, Ireland, France, Germany, Italy, Greece, and Switzerland for treatment of both recurrent and newly diagnosed GBM. (*Id.* at 96). It has been commercially available in the European Union since 2009. (*Id.*).

Glioblastoma is very rare, with approximately 10,000 cases annually in the US. (Exh. 4, p. 10). The National Institute of Health (NIH) designates GBM as a rare disease, with few treatment options. (*Id.*). GBM tumors are typically highly aggressive. (*Id.*). Survival at initial presentation is approximately 10 months, and upon recurrence, approximately 6 months, even with aggressive chemotherapy. (*Id.*). GBM is universally fatal and the disease is classified as “recurrent GBM” when the tumor recurs or progresses after standard treatment. (Exh. 2, p. 80). Appellant-Beneficiary had glioblastoma multiforme (GBM) of temporal lobe WHO grade IV, and was receiving concurrent chemoradiation therapy with temozolide. (Exh. 2, p. 20). In May 2017, Beneficiary had a brain scan which showed that he had a brain tumor. (Exh. 1, p. 27). He was operated and was diagnosed with a glioblastoma. (*Id.*). The surgery removed about 60% of the tumor. His treating physician prescribed the NovoTTF-100A System, which furnishes tumor treatment field therapy (“TTFT”) (Exh. 2, p. 20). In a letter of medical necessity dated June 18, 2018, his treating physician wrote a letter indicating that they have successfully used Optune in appropriately selected patients with GBM, and that he believes that Appellant-Beneficiary is a good candidate for treatment. (Exh. 1, p. 12). Optune is a prescription only, non-invasive device that is intended for continuous use throughout the day. (*Id.* at 13). Optune delivers TTF therapy, an electric field based loco-regional, antimitotic treatment modality. (*Id.*). TTF therapy has been shown to inhibit the growth of cancerous tumors in vitro and in vivo. (*Id.*). His treating physician wrote that patients suffering from GBM have limited treatment options, and that there are few if any available options that would benefit him in this clinical scenario. (*Id.*). Appellant-Beneficiary has exhausted essentially all FDA-approved treatments that could benefit him. (*Id.*). The treating physician specifically noted that Optune is his only viable treatment option, and that it is the only promising treatment option. (*Id.*). Patients suffering from GBM have limited treatment options. (*Id.* at 13). Appellant-Beneficiary started taking Optune on August 31, 2017, and he wrote that he felt great and that it is his best hope to control his brain tumor. (Exh. 1, p. 27). His doctor prescribed Optune given the aggressive nature and extremely limited options of his disease. (*Id.* at 27, 29-31). Patients diagnosed with glioblastoma on initial presentation have an expected survival of approximately 10 months, even with aggressive chemotherapy. (Exh. 3, p. 2). Beneficiary’s extended survival quantified the effectiveness of the Optune System given that he was not considered a candidate for further chemotherapy. (Exh. 4, p. 13).

Principles of Law

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("HHS"), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Social Security Act ("the Act") section 1869(b)(1)(A)). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. *See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The Administrative Law Judges ("ALJ's") within OMHA issue binding decisions of the Secretary, unless those decisions are later reviewed by the Medicare Appeals Council. *Id.* The calendar year 2018 AIC threshold amounts are \$160 for ALJ hearings. 82 Fed. Reg. 188 (Sept. 29, 2017)

B. Scope of Review

The issues before the ALJ include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a fully favorable decision he or she will notify the Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the Appellant and all the parties indicate in writing that they do not wish to appear before the ALJ at an oral hearing or if an examination of the record supports a finding in favor of the Appellant on every issue. 42 C.F.R. § 405.1038.

C. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. Section 557 of the Administrative Procedure Act and 70 Fed. Reg. 36386 (June 23, 2005). *De novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations on the claim and make an independent assessment in reliance upon the evidence and controlling laws. The burden of proving each element of a Medicare claim lies with the Appellant and is by preponderance of the evidence (i.e. satisfied through the submission of sufficient evidence in accordance with Medicare rules). *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, 1030.

Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a). The decision must be based on evidence offered at the hearing or otherwise admitted into in the record. (*Id.*).

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. *See* 42

C.F.R. § 405.1018. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries. *See* 42 C.F.R. § 405.1018(d).

II. Principles of Law

A. Social Security Act

Medicare Part B provides coverage to eligible beneficiaries for all or part of the cost of “medical and other health services,” a term which is defined by the Act as including, among many other things, durable medical equipment.” *Sections 1832(a)(1)(B) and 1861(s)(6) of Title XVIII of the Social Security Act; 42 C.F.R. §410.10(h).*

No Medicare payment can be allowed for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member *Section 1862(a)(1)(A) of Title XVIII of the Social Security Act; 42 C.F.R. §411.15(k)(2).*

No payment can be made to the provider or another person unless such information, as may be necessary, has been furnished in support of the medical necessity of the claimed services in order to determine the amount due such provider or other individual. *Section 1833 of Title XVIII of the Social Security Act; 42 C.F.R. §424.5(a)(6).*

When Medicare coverage is precluded under Section 1862(a)(1)(A), i.e., the item was not reasonable and necessary, payment will be made, notwithstanding the preclusion, when neither the individual who received the item nor the person who furnished the item knew or could reasonably be expected to know that the item was not covered. This provision is commonly referred to as the limitation of liability provision. *Section 1879 of Title XVIII of the Social Security Act, 42 C.F.R. §411.400.*

B. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than National Coverage Determinations, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. §405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals or local coverage determinations (“LCDs”). 42 C.F.R. § 405.1062 provides that Administrative Law Judges will give substantial deference to Local Coverage Determinations (LCDs) or Center for Medicare Services (“CMS”) program guidance when applicable. There is no applicable LCD in the instant case.

Analysis

After a review of the records, the undersigned ALJ finds that the preponderance of evidence showed that Appellant-Beneficiary met the Medicare coverage requirements for the electrical stimulation device at issue. In this case, Appellant-Beneficiary received an electrical stimulation device, NovoTTF-100A System (E0766) from December 30, 2017 to February 28, 2018. Optune, previously known as the NovoTTF-100A System, is a durable medical equipment that delivers alternating electric fields or tumor treating fields to the brain. (Exh. 4, p. 10). The device consists of an electric field generator which is connected to four insulated transducer arrays. (*Id.*). The arrays are placed on the patient's scalp and deliver the tumor treating fields therapy (TTF therapy) to the glioblastoma. (*Id.*). The fields slow the replication of the cancer cells or stop their growth altogether. (*Id.*). The fields may also destroy some of the cancer cells. (*Id.*). Optune is FDA-approved for recurrent and newly diagnosed GBM brain tumors. (*Id.*). Optune is a portable battery or power supply operated device, which may be carried by the patients in an over-the-shoulder bag or backpack and receive continuous treatment without changing their daily routine. (Exh. 2, p. 47). It is a portable, wearable medical device, and patients maintain normal daily activities while receiving TTF therapy continuously. (*Id.* at 80).

On January 1, 2014, CMS classified the Optune device as a DME requiring frequent and substantial servicing, which is billed under HCPCS code E0766, as a monthly rental through the duration of medical necessity. (Exh. 4, p. 11). The Optune System was the subject of numerous peer-reviewed published studies that demonstrate the safety and efficacy of the Optune System and TTF therapy generally. (*Id.* at 11). The studies are reported in some of the most prestigious journals in the country including the Journal of the American Medical Association. (*Id.*). Optune is included in the National Comprehensive Cancer Network (NCCN) guidelines for recurrent glioblastoma and for newly diagnosed GBM in combination with temozolomide. (*Id.*). In particular, for newly diagnosed glioblastoma, the NCCN guidelines (considered the gold standard for oncology management) give a level one recommendation for TTF therapy, i.e., a consensus exists among the experts based on the highest levels of evidence, that the treatment is recommended. (*Id.*). The Data Safety Monitoring Board for the clinical trial for the newly diagnosed glioblastoma (and patients that suffered recurrences during the trial) found the data so compelling, that they recommended early termination and allowing patients who were not receiving the treatment to be able to cross over and receive the treatment, deeming it unethical to withhold it, and the FDA agreed. (*Id.* at 12). It has widespread adoption and virtually every major payor in the United States covers the Optune System for individuals diagnosed with a glioblastoma. (*Id.* at 12). These payors include Highmark, Aetna, Anthem, Humana, Kaiser, UnitedHealthcare, Cigna, Harvard Pilgrim, Geisinger, HealthPartners, and several Blue Cross plans. (*Id.*). The FDA approved the NovoTT-100A system, under the pre-market approval (PMA) pathway in April 2011 (Exh. 2, pp. 80, 96). The PMA approval pathway is the most rigorous medical device approval pathway and is analogous to the FDA new drug application (NDA) pathway. (*Id.*). The FDA approved the device on the basis of results from a multi-center randomized controlled pivotal (phase III) trial. (*Id.*). The FDA PMA approval followed a positive vote from the FDA's Independent Medical Device Advisory Committee's Neurological Devices Panel. (*Id.*). The results of the study indicate that the NovoTTF-100A system produces clinically comparable outcomes to chemotherapy, but with fewer side-effects, including a reduced hospitalization rate and provides the patients with an improved quality of life (*Id.* at 111). Patients receiving chemotherapies suffer from wound healing complications, infections, diarrhea,

constipation, nausea, vomiting, pain, decreased blood cell counts and their complications, bleeding disorders and thromboembolic events (e.g. stroke). (*Id.* at 90). The manufacturer has applied the CE Mark to the device and received marketing approvals in the UK, Ireland, France, Germany, Italy, Greece, and Switzerland for treatment of both recurrent and newly diagnosed GBM. (*Id.* at 96). It has been commercially available in the European Union since 2009. (*Id.*).

Appellant-Beneficiary had glioblastoma multiforme (GBM) of temporal lobe WHO grade IV, and was receiving concurrent chemoradiation therapy with temozolide. (Exh. 2, p. 20). His treating physician prescribed the NovoTTF-100A System, which furnishes TTF therapy. (*Id.*). In a letter of medical necessity dated June 18, 2018, his treating physician wrote a letter indicating that they have successfully used Optune in appropriately selected patients with GBM, and that he believes that Appellant-Beneficiary is a good candidate for treatment. (Exh. 1, p. 12). Optune is a prescription only, non-invasive device that is intended for continuous use throughout the day. (*Id.* at 13). Optune delivers TTF therapy, an electric field based loco-regional, antimitotic treatment modality. (*Id.*). TTF therapy has been shown to inhibit the growth of cancerous tumors in vitro and in vivo. (*Id.*). His treating physician wrote that patients suffering from GBM have limited treatment options, and that there are few if any available options that would benefit Appellant-Beneficiary in this clinical scenario. (*Id.*). Appellant-Beneficiary has exhausted essentially all FDA-approved treatments that could benefit him. (*Id.*). The treating physician specifically noted that Optune is Appellant-Beneficiary's only viable treatment option, and that it is the only promising treatment option. (*Id.*). Patients suffering from GBM have limited treatment options. (*Id.* at 13). Optune is the only viable treatment option and that Appellant-Beneficiary has exhausted essentially all FDA-approved treatments that could benefit him in this current clinical scenario. (*Id.* at 13-14).

Glioblastoma is very rare, with approximately 10,000 cases annually in the US. (Exh. 4, p. 10). The National Institute of Health (NIH) designates GBM as a rare disease, with few treatment options. (*Id.*). GBM tumors are typically highly aggressive. (*Id.*). Survival at initial presentation is approximately 10 months, and upon recurrence, approximately 6 months, even with aggressive chemotherapy. (*Id.*). GBM is universally fatal and the disease is classified as "recurrent GBM" when the tumor recurs or progresses after standard treatment. (Exh. 2, p. 80). Appellant-Beneficiary's brain scan result in May 2017 showed that he had a brain tumor. (Exh. 1, p. 27). He was operated and he was diagnosed with a glioblastoma. (*Id.*). The surgery removed about 60% of the tumor, and afterwards he had radiation and chemotherapy and started taking chemotherapy pills. (*Id.*). He started taking Optune on August 31, 2017, and he wrote that he felt great and that it is his best hope to control his brain tumor. (*Id.*). His doctor prescribed Optune given the aggressive nature and extremely limited options of his disease. (*Id.* at 27, 29-31). Contrary to the QIC's decision, Appellant-Beneficiary's extended survival quantified the effectiveness of the Optune System, given that he was not considered a candidate for further chemotherapy. (Exh. 4, p. 13). In addition, hearing testimony from Appellant-Beneficiary's witness showed that the February 2018 MRI showed improvement in size of lesion as it was smaller, and that it proved that the Optune system was overall an effective treatment for Appellant-Beneficiary.

Medicare covers DME if it (1) meets the definition of DME; (2) is medically "reasonable and necessary" and (3) the equipment is used in the beneficiary's home. Medicare Benefit Policy Manual ("MBPM") (Pub. 100-02), Ch. 15, § 110. The regulations state that "CMS may consider for Medicare coverage" FDA approved devices "that have been categorized as non-experimental/investigational." 42 C.F.R. § 405.201(a) (2) (emphasis added). The regulations further clarify that CMS uses FDA categorization "as a factor in making Medicare coverage decisions." 42 C.F.R. § 405.201(a) (1) (emphasis added). Thus, under Medicare regulations, the fact that a device may be deemed non-experimental/investigational by virtue of its FDA classification means, as a threshold matter, only that it is eligible to be considered for Medicare coverage. Accordingly, the FDA clearance that the NovoTTF-100A system obtained does not, by itself, establish that the device meets Medicare coverage requirements, i.e., that it has been shown to be a medically reasonable and necessary treatment for GBM. Nevertheless, the undersigned ALJ finds that the evidence as shown in the records, establishes that at the time the device was furnished, the Optune system had gained general acceptance within the medical community in the treatment of GBM; and thus, meets medical necessity standards for Medicare coverage. Moreover, the DMAC Medical Directors indicated in the letter dated August 7, 2018, that they do not believe that newly diagnosed GBM is addressed by LCD L34823. In this case, Appellant-Beneficiary had a newly diagnosed GBM. Furthermore, the undersigned ALJ concurs with the Appellant-Beneficiary's representative that in the face of widespread acceptance in the medical community and in the face of robust support for the Optune system's effectiveness for a disease that is notoriously difficult to treat, the LCD should not be used to preclude Medicare coverage of a device that meets Medicare coverage criteria. In addition, Appellant-Beneficiary's extended survival and reduction in the size of the lesion as shown in the February MRI, quantified the effectiveness of the Optune System given that he was not considered a candidate for further chemotherapy. Considering the foregoing, the preponderance of evidence showed that Medicare coverage exists for the electrical stimulation device, NovoTTF-100A System (E0766) provided to the Appellant-Beneficiary on the dates of service at issue, and that Appellant-Beneficiary met the Medicare criteria for coverage.

Conclusions of Law

Medicare coverage exists for the electrical stimulation device, NovoTTF-100A System (E0766) provided to the Appellant-Beneficiary on the dates of service at issue, and the Appellant-Beneficiary is entitled to payment.

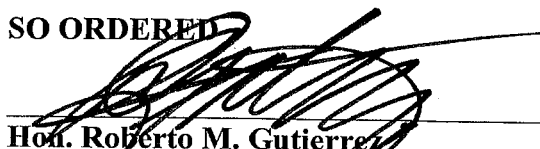
Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

Dated:

DEC 28 2018

SO ORDERED


Hon. Roberto M. Gutierrez
U.S. Administrative Law Judge



**UNITED STATES DEPARTMENT
OF
HEALTH AND HUMAN SERVICES**
OFFICE OF MEDICARE HEARINGS AND APPEALS
SOUTHERN FIELD OFFICE
Miami, Florida

Appeal of:	ALJ Appeal No.: 1-2669116429
Beneficiary:	Medicare Part C
HICN: XXX-XX-1085A	Before: Lauren Heard U.S. Administrative Law Judge

ADMINISTRATIVE LAW JUDGE DECISION AND ORDER

I. SUMMARY OF DECISION

After carefully considering the evidence and arguments presented, a **Favorable** decision is entered for the Beneficiary, ("Beneficiary" or "you") who is also the Appellant. As set forth in more detail herein, the Humana Medicare Employer PPO Medicare Advantage Plan offered by Humana Insurance Company, ("Plan") incorrectly denied coverage for an electrical stimulation device used for cancer treatment, and specifically treatment with the NovoTTF-100APlus Transducer ("Device"). Therefore, the Beneficiary is entitled to Plan benefits for treatment with the Device pursuant to physician orders.

II. PROCEDURAL HISTORY

The Plan received a request for prior authorization for treatment with the Device coded as durable medical equipment ("DME") pursuant to HCPCS Code E0766 (Electrical stimulation device used for cancer treatment, includes all accessories, any type) from the Device Supplier, Novocure, ("Supplier") on behalf of the Beneficiary. The Supplier indicates a willingness to offer a discount off the list price for the device via a negotiated letter of agreement for in network benefits. *Ex. 4, pp. 27-33.*¹ With its request for authorization, the Supplier presents a statement from Dr. REDACT MD who identifies himself as the Beneficiary's physician. Dr. REDACT requests authorization to "initiate treatment with the Device at Norton Hospital – Kentucky Cancer Institute," which is indicated to be a facility which played a role in clinical trials for the device "and was one of the first hospitals in the nation to obtain manufacturer certification to use the

¹ The Device is coded E0766. The Medicare Pricing, Data Analysis and Coding Contractor, Noridian Healthcare Solutions website confirms that this code does not appear on the CMS National Fee Schedules available in DMECS, and that "If you would like instructions on how to bill this product, contact your DME MAC for pricing assistance." www.dmeprdac.com, (11/6/14)

device commercially following its FDA approval.” *Ex. 4, p. 28*. Dr. REDACTED indicates that the Device is a prescription only, non-invasive device that is intended for continuous use throughout the day by the patient. *Ex. 4, p. 29*.

The file does not reflect the original Plan denial, but does include the request for redetermination filed by the Supplier as the appointed representative of the Beneficiary. Therein, the Supplier argues that the Device is FDA approved for the Beneficiary’s condition, glioblastoma multiforme (GBM), attaching among other things medical records and a letter of medical necessity from REDACTED PA to Dr. REDACTED of Norton Hospital – Norton Cancer Institute. *Ex. 4, pp. 22-26*.

On redetermination, the Plan again denied coverage, stating that the diagnosis was glioblastoma for which authorization of electrical stimulation device used for cancer treatment, including supplies, has been requested. The Plan acknowledged that the medical record indicates the member has failed other treatments for brain cancer. However, the Plan again denied payment because Local Coverage Determination L34730 for New Hampshire, titled “Tumor Treatment Field Therapy (TTFT)” indicates that “Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.” *Ex. 4, pp. 13-14.A*

As required pursuant to Medicare rules, the Plan forwarded the denial to the Independent Review Entity, (also called the Part C QIC) Maximus Federal Services, who again denied the claim on the grounds that LCD L34730 provides that treatment with the device is not reasonable and necessary.

On or about September 14, 2014, the Part C QIC received a request for Administrative Law Judge (“ALJ”) hearing filed by the Supplier as the Beneficiary’s representative, which was forwarded to the Office of Medicare Hearings and Appeals on September 24, 2014. The request was timely and the amount in controversy satisfies the jurisdictional requirement for an ALJ hearing pursuant to Title XVIII of the Social Security Act (the “Act” or “Title XVIII”) Sections 1852(g)(5) and 1869(b)(1)(E).

A telephonic hearing was held on November 3, 2014. The Beneficiary and his wife REDACTED were present and testified. In addition, the Supplier’s representatives, Justin Kelly, Sr. Director of Health Policy and Payment, and Dan McCoy, Case Manager, appeared and/or testified on behalf of the Beneficiary. Dr. REDACTED the Beneficiary’s current treating oncologist, also appeared and testified on behalf of the Beneficiary. The Plan was represented Dr. Kathleen O’Connell, MD, Medical Director and Katrina Jewell, Medicare Grievance & Appeals Specialist. Exhibits 1 – 12 have been admitted into evidence. Good cause is found for the admission of new documentation submitted to the ALJ, due to the need for updated documentation concerning the Device efficacy, and ongoing treatment of the Beneficiary and need for review of updated medical records to determine the current medical need of the Beneficiary for the Device related to this request for prior authorization. See 42 C.F.R. §§405.1018, 1028 (requiring a finding of good cause to admit evidence first submitted at ALJ level or appeal).

III. ISSUES

The issue is whether the Plan must authorize coverage for the treatment with the NovoTTF-100APlus Transducer Device, coded by HCPCS Code E0766, i.e. is the Device covered and payable by the Plan pursuant to Section 1851 et seq. of Title XVIII (Medicare Part C).

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IV. LEGAL FRAMEWORK

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§ 1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services, or CMS. Title 42 of the Code of Federal Regulations, (“C.F.R.”), Chapter IV contains implementing regulations. Centers for Medicare and Medicaid Services, (“CMS”) Rulings and Manual Guidance and National and Local Coverage Determinations may also be cited herein, when applicable.²

I. ALJ Review Authority

Plan determinations are subject to appeals procedures set forth under the Medicare Advantage Program, also known as Medicare Part C.

A. Jurisdiction

An enrollee who receives an adverse Medicare Advantage (“MA”) plan determination, including the MA organization’s refusal to provide or pay for services in whole or part, is entitled to a Reconsideration by the MA organization, and if not thereafter satisfied, to a subsequent Reconsideration to be performed by an Independent Review Entity, or, IRE. *See Section 1852(g) of Title XVIII; 42 C.F.R. §§422.566; 422.576-596.*

Enrollees or providers dissatisfied with the IRE’s Reconsideration are entitled to a hearing before the Secretary of the Department of Health and Human Services (“HHS”), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. *See Section 1852(g)(5) of Title XVIII; 42 C.F.R. §§422.600-602.*

In implementing this statutory directive, the Secretary has delegated her authority to administer the nationwide hearings and appeals system for the Medicare program to the Office of Medicare Hearings and Appeals (“OMHA”). *See 70 Fed. Reg. 36386-36387 (June 23, 2005); See also 42 C.F.R. §§422.600-602.*

The Administrative Law Judges, ALJs, within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.; See also 42 C.F.R. §422.608.* The parties to the ALJ hearing may include the plan enrollee (also referred to herein as the beneficiary or member), an assignee of the enrollee (that is, a physician or other provider who has furnished a service to the enrollee and formally agrees to waive any right to payment from the enrollee for that service), the legal representative of a deceased enrollee’s estate, the MA organization (i.e. the Plan), and any other person, provider or entity whose rights may be affected by the hearing as determined by the ALJ or at any lower level of appeal. *See 42 C.F.R. §422.602(c); See also 422.574; 422.582(d); 422.592(c).*

The request for an ALJ hearing is timely if filed within sixty days after receipt of a Reconsideration issued by the IRE. *See 42 C.F.R. §422.602.* To be entitled to an ALJ hearing, a party must meet the minimum amount in controversy requirement of \$100; however, this minimum is subject to increases which are published in the Federal Register. *42 C.F.R. §§405.1006; 422.600.* The amount in controversy threshold for ALJ hearing requests filed during 2014 is \$140. *78 Fed. Reg. 59702-59704 (September 27, 2013).*

² Many of the sources cited herein are available at www.cms.gov.

B. Scope of Review

In hearing appeals under Medicare Part C, the ALJ generally applies the same administrative review and hearing processes that are employed in reviewing cases under Original Medicare Parts A and B. 42 C.F.R. §422.562(d). Thereunder, the ALJs conduct *de novo* hearings.³ See 70 Fed. Reg. 36386, 36387 (June 23, 2005); 42 C.F.R. §405.1000(d). The issues before the ALJ include all the issues brought out in the Plan determination, Plan reconsideration or IRE reconsideration that were not decided entirely in the appellant's favor. However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, notice will be sent to the appellant and it will be considered at the hearing. See 42 CFR 405.1032.

All laws, regulations and Centers for Medicare and Medicaid Services ("CMS") rulings pertaining to the Medicare and Medicaid programs, including, but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations are binding on ALJs. 42 C.F.R. §405.1063.

The Administrative Law Judge's, or ALJ's, application of National Coverage Determinations ("NCDs"),⁴ written coverage decisions of Medicare contractors, also called Local Coverage Determinations, or LCDs⁵, and CMS manual guidance is also addressed under Medicare law. Section 1871(a)(2) of Title XVIII provides that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. Medicare Regulations at 42 C.F.R. 405.1060,4, provide that an applicable NCD is binding on ALJs. Medicare Regulations at 42 CFR §405.1062 provide that in making coverage determinations ALJs will give substantial deference to policy guidance including applicable LCDs or CMS program guidance, such as program memoranda and manual instruction. However, an ALJ is not required to follow such policy guidance. An explanation in the decision is required if the ALJ does not follow such policy guidance.

II. Medicare Part C – Medicare Advantage Plan Coverage

A. General Framework for Medicare Part C

Section 1851 et seq. of Title XVIII establishes the Medicare Advantage Program, also referred to as Medicare Part C, which permits eligible individuals to receive Medicare benefits through enrollment in a private health insurance plan, typically referred to as a Medicare Advantage, or MA plan.

Medicare Regulations at 42 C.F.R. Part 422 provide rules governing the Medicare Advantage Program.

³ In a *de novo* review, the ALJ conducts a new and independent review of the record and is not bound by any previous decision(s) issued in a case.

⁴ An NCD is a determination by the Secretary of whether a particular item or service is covered nationally. See 42 C.F.R. §405.1060.

⁵ An LCD is an Original Medicare Part A or B contractor-wide written policy coverage determination as to whether particular items or services are medically reasonable and necessary. See 42 C.F.R. §400.202.

Medicare Managed Care Manual, Pub. 100-16, ("CMS Pub. 100-16") also offers guidance regarding the Medicare Advantage Program.

This authority explains that the benefits offered by an MA plan are reviewed and approved by CMS to ensure that Medicare guidelines have been met. 42 C.F.R. §§422.100(f); CMS Pub. 100-16, Ch. 4, §10.2.1. The plan provides eligible enrollees, at a minimum, basic benefits, which include all medically necessary Medicare covered Part A and Part B services, except hospice services, certain clinical trial services and certain service during inpatient stays during which MA plan enrollment begins or ends. MA plans may also include mandatory and/or optional supplementary benefits. See *Id.*; 42 C.F.R. §§422.100(a), (c); 422.101(a).⁶

With respect to the required Original Medicare benefits, a Medicare Advantage Organization, or MAO (i.e. the plan)

An MA organization (MAO) offering an MA plan must provide enrollees in that plan with all Part A and Part B, Original Medicare services, if the enrollee is entitled to benefits under both parts, and Part B services if the enrollee is a grandfathered "Part B only" enrollee. The MAO fulfills its obligation of providing Original Medicare benefits by furnishing the benefits directly, through arrangements, or by paying on behalf of enrollees for the benefits.

Administration of the Medicare program is governed by Title XVIII of the Social Security Act (the Act). Under the Medicare program, the scope of benefits available to eligible beneficiaries is prescribed by law and divided into several main parts. Part A is the hospital insurance program and Part B is the voluntary supplementary medical insurance program.

The scope of the benefits under Part A and Part B is defined in the Act. The scopes of Part A and Part B are discussed in sections 1812 and 1832 of the Act, respectively, while section 1861 of the Act lays out the definition of medical and other health services. Specific health care services must fit into one of these benefit categories, and not be otherwise excluded from coverage under the Medicare program (see §1862 for exclusions).

In general, the Act lists categories of items and services covered by Medicare, although Congress occasionally adds specific services to be covered by Medicare. Some categories are defined more broadly than others; for example, the Act includes hospital outpatient services furnished incident to physicians' services (§1861(s)(2)(B)) but also specifically includes diabetes screening tests (§1861(s)(2)(Y)). The Act vests in the Secretary the authority to make determinations about which specific items and services, within categories, may be covered under the Medicare program. Further interpretation is provided in the Code of Federal Regulations and CMS guidance.

Medicare coverage and payment is contingent upon a determination that:

- A service is in a covered benefit category;

⁶ Medicare Part D prescription drug benefits may also be offered through MA organizations in conjunction with their MA plan. See 42 C.F.R. §§422.4(c).

- * A service is not specifically excluded from Medicare coverage by the Act; and
- * The item or service is "reasonable and necessary" for the diagnosis or treatment of an illness or injury or to improve functioning of a malformed body member, or is a covered preventive service.

CMS Pub. 100-16, Ch. 4, §10.2.

In addition to providing Original Medicare benefits, to the extent applicable, the Medicare advantage organization, or MAO, also furnishes, arranges, or pays for supplemental benefits and prescription drug benefits to the extent they are covered under the plan. *CMS Pub. 100-16, Ch. 4, §10.2.1.*

There are three basic types of MA plans open to all MA-eligible Medicare beneficiaries residing in the authorized service area of the plan include: (1) Coordinated Care Plans, or CCPs, (2) Private Fee-For Services, or PFFS, plans, and (3) Medical Savings Account, or MSA, plans. *See 42 C.F.R. §422.4; CMS Pub. 100-16, Ch. 1, §§30.1-30.2.2.* A CCP is a plan that includes a network of providers that are under contract or arrangement with the organization to deliver the benefit package approved by CMS. The CCP network is approved by CMS to ensure that all applicable requirements are met, including access and availability, service area, and quality requirements. A PPO such as provides coverage for the Beneficiary in this case has a network of providers that have agreed to a contractually specified reimbursement for covered benefits with the organization offering the plan; and, provides for reimbursement for all covered benefits regardless of whether the benefits are provided within the network of providers; only for purposes of quality assurance requirements in §422.152(e), is offered by an organization that is not licensed or organized under State law as an HMO; and, does not permit prior notification for out-of-network services — that is, a reduction in the plan's standard cost-sharing levels when the out-of-network provider from whom an enrollee is receiving plan-covered services voluntarily notifies the plan prior to furnishing those services, or the enrollee voluntarily notifies the PPO plan prior to receiving plan-covered services from an out-of-network provider. *See Id.; CMS Pub. 100-16, Ch. 1, §§30.2.3.*

Medicare Regulations at 42 C.F.R. §422.11 state that an MA plan must disclose the benefits offered under a plan, including applicable conditions and limitations, premiums and cost-sharing (such as copayments, deductibles, and coinsurance) and any other conditions associated with receipt or use of benefits to its enrollees. This information may be found in the MA Plan Evidence of Coverage, ("EOC"), which MA plans provide to enrollees upon enrollment, on an annual basis and through the plan's internet web site. These disclosure rules are also discussed in CMS Pub. 100-16, Ch. 3. All such marketing materials used by plan sponsors or their subcontractors must be submitted by the plan sponsor (or its designee) to CMS for review and approval (or acceptance). *See CMS Pub. 100-16, Ch. 3, §30.5.*

In making benefit determinations, the MA organization complies with CMS's national coverage determinations (NCDs), general coverage guidelines included in CMS's Medicare manuals and instructions (unless modified by Federal regulations or related instructions), and applicable written coverage decisions of Original Medicare contractors (e.g. LCDs) with jurisdiction for claims in the geographic area in which such services are covered under the MA plan. (If an MA plan covers

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geographic areas encompassing more than one local coverage policy area, the MA organization offering such an MA plan may elect to apply to plan enrollees in all areas uniformly the coverage policy that is the most beneficial to MA enrollees.) *See* 42 C.F.R. §422.101(b).

B. Plan Evidence of Coverage (EOC)

Because the Plan discloses its covered benefits in its Evidence of Coverage, or EOC, it is necessary to review that document to determine policy coverage. In pertinent part, your Plan EOC states that services that are covered for you include "[d]urable medical equipment (DME) and related supplies." Prior authorization is required requested when you get the item out of network, and required when you get the items in network or "for any DME item over \$750." *EOC*, pp. 63-64, Chapter 4, Section 2.1, Medical Benefits Chart. A 4% coinsurance is required when you get the services at a durable medical equipment provider, whether in or out of network. *Id.*

Your EOC further explains that

- "Your Medicare covered services must be provided according to the coverage guidelines established by Medicare." *EOC*, p. 53, Chapter 4, Section 2.1.
- "Except in the case of preventative services and screening tests, your services (including medical care, services, supplies, and equipment) must be medically necessary. 'Medically necessary' means that the services, supplies, or drugs are needed for the prevention, diagnosis, or treatment of your medical condition and meet accepted standards of medical practice." *Id.*

C. Pertinent Original Medicare Coverage Rules

Because Medicare rules provide that your Medicare Part C Medicare advantage plan must include benefits provided under and according to Medicare coverage guidelines established by Original Medicare Parts A and B, it is also instructive to review those guidelines, as established by statute, regulation, NCD, LCD and CMS manual guidance.

Sections 1831 et seq. of Title XVIII establish the Supplementary Medical Insurance Benefits for the Aged and Disabled (Medicare Part B). Section 1832 of Title XVIII and Medicare Regulations at 42 C.F.R. §410.3 establish the scope of benefits that are provided to eligible beneficiaries under the Medicare Part B insurance program, which includes "medical and other health services." Sections 1832(a)(1), 1861(n),(s)(6) and 1834(a)(13) of Title XVIII and Medicare Regulations at 42 C.F.R. §410.38(a) provide that covered "medical and other health services" under Medicare Part B include, among many other things, the rental or purchase of durable medical equipment ("DME"), if the equipment is used in the patient's home or in an institution that is used as a home.

Section 1862(a)(1)(A) of Title XVIII provides that "[n]otwithstanding any other provision of the Act, no payment shall be made for any expenses incurred for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." *See also* 42 CFR §411.15(k).

The Manuals issued by the Centers for Medicare & Medicare Services ("CMS") serve to clarify and explain the various coverage requirements stated in the statute and regulations.

Medicare National Coverage Determinations Manual, Pub. 100-03 ("CMS Pub. 100-03"), Ch. 1, includes National Coverage Determinations. CMS Pub. 100-03, Ch. 1, §280.1 explains that the term Durable Medical Equipment, or DME, is defined as equipment which:

- Can withstand repeated use; i.e., could normally be rented, and used by successive patients;
- Is primarily and customarily used to serve a medical purpose;
- Generally is not useful to a person in the absence of illness or injury; and
- Is appropriate for use in a patient's home.

Medicare Benefit Policy Manual, Pub. 100-02 ("CMS Pub. 100-02"), Ch. 15, §110, also provides guidance pertaining to Medicare coverage of DME, and explains that:

Expenses incurred by a beneficiary for the rental or purchases of durable medical equipment (DME) are reimbursable if the following three requirements are met:

- The equipment meets the definition of DME [see above];
- The equipment is necessary and reasonable for the treatment of the patient's illness or injury or to improve the functioning of his or her malformed body member (§110.1); and
- The equipment is used in the patient's home.

CMS Pub. 100-02, Ch. 15, §110(c) provides guidance as to the "necessary and reasonable" requirement, and states as follows:

Although an item may be classified as DME, it may not be covered in every instance. Coverage in a particular case is subject to the requirement that the equipment be necessary and reasonable for treatment of an illness or injury, or to improve the functioning of a malformed body member. These considerations will bar payment for equipment which cannot reasonably be expected to perform a therapeutic function in an individual case or will permit only partial therapeutic function in an individual case or will permit only partial payment when the type of equipment furnished substantially exceeds that required for the treatment of the illness or injury involved.

1. Necessity for the Equipment

Equipment is necessary when it can be expected to make a meaningful contribution to the treatment of the patient's illness or injury or to the improvement of his or her malformed body member. In most cases the physician's prescription for the equipment and other medical information available to the DMERC will be sufficient to establish that the equipment serves this purpose.

2. Reasonableness of the Equipment

Even though an item of DME may serve a useful medical purpose, the DMERC or intermediary must also consider to what extent, if any, it would be reasonable for the Medicare program to pay for the item prescribed. The following considerations should enter into the determination of reasonableness:

1. Would the expense of the item to the program be clearly disproportionate to the therapeutic benefits which could ordinarily be derived from use of the equipment?

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2. Is the item substantially more costly than a medically appropriate and realistically feasible alternative pattern of care?
3. Does the item serve essentially the same purpose as equipment already available to the beneficiary?

3. Payment Consistent With What is Necessary and Reasonable

Where a claim is filed for equipment containing features of an aesthetic nature or features of a medical nature which are not required by the patient's condition or where there exists a reasonably feasible and medically appropriate alternative pattern of care which is less costly than the equipment furnished, the amount payable is based on the rate for the equipment or alternative treatment which meets the patient's medical needs.

The acceptance of an assignment binds the supplier-assignee to accept the payment for the medically required equipment or service as the full charge and the supplier-assignee cannot charge the beneficiary the differential attributable to the equipment actually furnished.

4. Establishing the Period of Medical Necessity

Generally, the period of time an item of durable medical equipment will be considered to be medically necessary is based on the physician's estimate of the time that his or her patient will need the equipment. See the Medicare Program Integrity Manual, Chapters 5 and 6, for medical review guidelines.

Local Coverage Determination L34730, titled "Tumor Treatment Field Therapy (TTFT)" issued by Medicare DME Contractor NHIC Corp., ("LCD L34730") states "Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary." The pertinent Local Coverage Determinations, or LCDs, and related Policy Article A52680, also issued by Medicare DME Contractor NHIC Corp., are further addressed below under Findings of Fact.

Medicare Program Integrity Manual, Pub. 100-08 ("CMS Pub. 100-08"), Ch. 5, also provides guidance as to documentation requirements to support that Medicare coverage criteria for items of DME have been met. Chapter 5, Section 5.7 states as follows, in pertinent part:

For any DMEPOS item to be covered by Medicare, the patient's medical record must contain sufficient documentation of the patient's medical condition to substantiate the necessity for the type and quantity of items ordered and for the frequency of use or replacement (if applicable). The information should include the patient's diagnosis and other pertinent information including, but not limited to, duration of the patient's condition, clinical course (worsening or improvement), prognosis, nature and extent of functional limitations, other therapeutic interventions and results, past experience with related items, etc. . . . neither a physician's order nor . . . a supplier prepared statement nor a physician attestation by itself provides sufficient documentation of medical necessity, even though it is signed by the treating physician or supplier. There must be information in the patient's medical record that supports the medical necessity for the item and substantiates the answers on the CMN [certificate of medical necessity] (if applicable) or DIF [DME information form] (if applicable) or information on a supplier prepared statement or physician attestation (if applicable).

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V. FINDINGS OF FACT

The medical record

The record as received from the Independent Review Entity, Maximus, includes a prescription and order for the Device signed by Dr. REDACTED who is a board certified neuro-oncologist (as confirmed by the testimony of Dr. REDACTED), for use by the Beneficiary for six months for treatment for the Beneficiary's diagnosis of Glioblastoma Multiforme, identified by ICD-9 code 191.9 (Malignant neoplasm of brain, unspecified), with a requested start date of September 3, 2014. *Ex. 3, p. 1.* (The record indicates that treatment has not, in fact, commenced pending the outcome of this appeal.) This medical record includes an August 13, 2014 progress note from Dr. REDACTED indicating that the Beneficiary "is [here] for a follow up brain MRI." *Ex. 3, p. 2.* The progress note states that the Beneficiary has a diagnosis of GBM, and states "Oncology Treatment Summary: Previous Therapy, Craniotomy x2, Radiation x2, Avastin." *Id.* The progress note further identifies that concurrent radiation treatment plus chemotherapy with Temodor was completed on June 15, 2012, with Temodor induced thrombocytopenia during radiation treatment documented. Specifically, a post-radiation treatment challenge with low dose of Temodor resulted in thrombocytopenia and discontinuation of Temodor. *Id.* In the August 13, 2014 progress note, Dr. REDACTED indicates that a neurological examination revealed the Beneficiary to be much more fatigued, with left optic neuropathy with light and color desaturation out of proportion to the Beneficiary's cataract. Dr. REDACTED identifies a Diagnosis/Assessment/Plan including "1. GBM: multiple surgeries, Radiation course x2, Avastin (chemotherapy-induced bone marrow failure). He is unfortunately slowly failing. He is not a candidate for further surgery or Chemotherapy. I reviewed with them the Novo-TFF: he would like to be considered for it." *Ex. 3, p. 4.*

In the progress note, Dr. REDACTED further indicates "I brought up today's [August 13, 2014 MRI] films and reviewed with them: there is progression the T2 flair without change in contrast enhancement. This is the pattern commonly seen with early Avastin failure." *Ex. 3, p. 4.* The August 13, 2014 MRI report itself indicates no recurrent GBM was shown, but does confirm the T2 anomaly addressed by Dr. REDACTED as follows:

- "1. No evidence of new or progressive nodular enhancement to suggest recurrent glioblastoma.
2. There is progressive T2 prolongation within the left cerebrum in a both diffuse as well as focal pattern. The diffuse progression is seen within the corona radiata and centrum semiovale and this represents a slight gradual progression over the series of recent postoperative MRIs dating to 2013. This has the appearance of likely treatment-induced vasculopathy.
3. There are progressive more focal regions of increased T2 signal seen within the anterior aspect of the left lentiform nuclei and internal capsule. Based on absence of mass effect and appearance of progressive treatment related vasculopathy rather than recurrent disease. Continued standard MRI imaging follow-up is recommended.
4. Improving postoperative subdural hematoma which now has the appearance of chronic postoperative meningeal thickening. No new hemorrhage or progressive hemorrhage is identified."

Ex. 3, pp. 5-7.

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A more recent October 13, 2014 MRI report has now been submitted, which indicates an impression of a "new 1.3-cm enhancing nodule in the left temporal stem; new 1.0-cm T2 hyperintense lesion in the left subinsular white matter. These lesions are concerning for disease progression." Ex. 8. With the new MRI report, an October 13, 2014 progress note from the Beneficiary's new neuro-oncologist, Dr. REDACTED (who also testified at the hearing) has been submitted on behalf of the Beneficiary. (At the hearing, Ms. REDACTED confirmed that Dr. REDACTED has taken over the Beneficiary's care from Dr. REDACTED, who is no longer available to the Beneficiary - Dr. REDACTED left"). Dr. REDACTED's progress note describes the results of the October 13, 2014 MRI and also includes a review of the Beneficiary's medical history, generally consistent with the above earlier presented documentation, but with additional details and an updated medical status of the Beneficiary. Ex. 9.

In his October 13, 2014 progress note, as confirmed by his testimony at the hearing, Dr. REDACTED explains that the Beneficiary is a 67 year old diagnosed on April 2012 with a left temporal gliosarcoma/glioblastoma multiforme. The Beneficiary underwent surgery at that time, and subsequently received radiation together with Temozolomide, also called Temodor, (which the hearing testimony confirms is chemotherapy) treatment with a completion date of June 2012, complicated by thrombocytopenia resulting in discontinuation of Temozolomide. The Beneficiary subsequently remained stable until May of 2013, at which time there was MRI evidence of recurrence of the initial tumor. On July 26, 2013, the Beneficiary underwent neurosurgical re/resection. The concurrent pathology report histologically confirmed glioblastoma in the specimen removed from the Beneficiary's left temporal lobe, which Dr. REDACTED confirmed at the hearing would be considered a recurrence in the supratentorial region of the brain after receiving chemotherapy.⁷ The Beneficiary then suffered a subdural hematoma following a fall, and received additional palliative radiation therapy from November 18 through December 4, 2013 together with Avastin. Dr. REDACTED further confirmed that Avastin is not considered a chemotherapy treatment, but is FDA approved for patients with GBM. Dr. REDACTED also confirmed that although Avastin does not induce bone marrow suppression typical of chemotherapy treatments, it does have other side effect including fatigue. An MRI from March of 2014 then showed that the Beneficiary was stable. A following MRI from August 13, 2014 (identified above) was described by Dr. REDACTED in his progress note as demonstrating no new or progressive nodular enhancement, though the Beneficiary was experiencing progressive fatigue and a decision was made to discontinue Avastin. Ex. 9. At the hearing, Dr. REDACTED further explained that the T2 flair shown in the August 13, 2014 MRI could be considered evidence of early progression of the disease, though not blatant evidence of such.

In his October 13, 2014 progress note, Dr. REDACTED also describes the results of the October 13, 2014 MRI as indicating progression of the disease (glioblastoma multiforme), with a plan to reinstitute Avastin and continue attempts to obtain the Device at issue in this hearing. Ex. 9. I find that this medical record serves to confirm the hearing testimony of Dr. REDACTED that surgical (x2)

⁷ Subsequent to the hearing, additional progress notes were submitted generally supportive of Dr. REDACTED testimony and medical history included in his October 13, 2014 progress note, including: a July 26, 2013 operative report pertaining to a left temporal craniotomy for resection of tumor and associated pathology report confirming glioblastoma in the specimen removed from the left temporal mass. Ex. 11.

and radiation (also x2) options have been exhausted for treatment of the Beneficiary's GBM. Dr. REDACTED further expressed his concurrence at the hearing with the earlier decision of Dr. REDACTED to try to proceed with the Device given the Beneficiary's medical history in this case. D

TTF Treatment and Literature

Pursuant to an informal benefit category determination (BCD) issued by the CMS Director of DMEPOS Policy on July 26, 2013, the NovoTTF-100A System is a non-invasive system used in the patient's home that delivers tumor treating fields therapy to the brain to disrupt rapid cell division exhibited by recurrent GBM tumors, comprised of a durable electrical field generator and disposable insulated transducer arrays for use with the generator which meets the Medicare definition of durable medical equipment (DME) in that it: can withstand repeated use; has an expected life of at least three years; is primarily and customarily used to serve a medical purpose; generally is not useful to a person in the absence of an illness or injury; and is appropriate for use in the home. *Ex. 12, p. 12. See also Policy Article A52680* (indicating that tumor field therapy devices are covered under the Medicare DME benefit, so long as other requirements such as reasonable and necessary requirements are met).

The submitted Novocure "NOVOTTF-100A System Product Dossier," found at Exhibit 2 in the file, identifies that this product is an FDA Approved Treatment for Recurrent Glioblastoma Multiforme, and includes technical information and studies related to this FDA approval. The Dossier' bibliography cites articles and studies as sources, with dates from 1995 through 2012. *Ex. 2, pp. 46-48.* The bibliography also refers to the 2011 FDA approved Instructions for Use and the Summary of Safety and Effectiveness Data for the NovoTTF-100A System. Appendix A to the Dossier identifies an FDA April 8, 2011 Premarket Approval letter, which states as follows:

Indication for Use: The NovoTTF-100A is intended as a treatment for adult patients [22 years of age or older] with histologically-confirmed glioblastoma multiform (GBM), following histologically – or radiologically-confirmed recurrence in the supra-tentorial region of the brain after receiving chemotherapy. The device is intended to be used as monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted.

Ex. 2, p. 23.

This approval language is confirmed by the undersigned ALJ as included in the FDA's April 8, 2011 premarket approval letter, as available on at www.fda.gov.⁸ The testimony of the Supplier's representative, Mr. Kelly, confirms that the post-approval study required by the premarket approval letter is currently underway with patients at multiple sites throughout the United States. Mr. Kelly further confirmed that the approval language remained in effect as of the date of the hearing, and had not been modified by the FDA.

⁸ An ALJ may obtain information that is publicly available, including information that is available to the general public via the Internet or in a printed publication such as, but not limited to, information available on a CMS or contractor Web site or information in an official CMS or DHHS publication (such as, but not limited to, provisions of NCDs or LCDs, procedure code or modifier descriptions, fee schedule data, and contractor operating manual instructions). *See 42 C.F.R. §405.1034.*

Mr. Kelly further confirmed at the hearing that in the Pivotal Trial relied upon by the Supplier to substantiate the safety and effectiveness of the Device, the median duration of treatment was 2.3 months, whereas in the Supplier's patient registry just published or to be published in the journal *Seminars on Oncology*, this was closer to 4 months. These patients wore the Device until the physician determined that it was inappropriate for them to do so. Mr. Kelly further confirmed that the Device was for home use of 18 hours per day, pursuant to the FDA approved labeling.

The submitted literature from the Supplier also includes copies of several articles and studies. Among this material, for example, is a 2012 overview by Gutin and Wong, (noted as funded by the Supplier, Novocure). This overview first reviewed studies of the Device as a monotherapy. In this respect, the Device was first applied to patients in a small feasibility trial in 2003, was involved in a pilot trial in 2004, and a further pivotal phase III, multicenter, randomized clinical study of 237 recruited patients from 2006 through 2009. The authors conclude that based on the results of the pivotal phase III study, the FDA approved the NovoTTF-100A, device on April 8, 2011, through the pre-market approval regulatory pathway. The authors note that the FDA concluded that the study results showed the Device to be comparable in efficacy to active chemotherapy, without many of the side effects associated with chemotherapies and with a better quality of life. The authors also review two studies of combined TTF therapy and chemotherapy, which were described by the authors as "promising." The authors concluded that TTF therapy has a superior safety profile with side effects that did not appear to overlap with other treatments, and that the rational combination of TTF therapy with specific pharmacologic agents may enhance tumor cell death because of potential additive or synergistic effects. The authors acknowledged that additional research could shed light on the optimal scheduling to achieve a synergistic effect on tumor growth leading to long-term tumor control and enhanced patient survival. *Ex. 2, pp. 65-71.*

At the hearing, Dr. REDACTED also referenced a Stupp, Wong et al. study (a copy of which is included in the record) first published in the *European Journal of Cancer*,⁹ which concluded that NovoTTF-100A for Tumor Treatment Fields (TTF) therapy appeared to be comparable in efficacy and activity to chemotherapy regimens that are commonly used for recurrent glioblastoma, while toxicity and quality of life clearly favored TTF. *Ex. 2, pp. 42-59.*

Dr. REDACTED further testified that after Avastin failure, or in the Beneficiary's case supreme intolerance of the drug, the probability of any chemotherapeutic agent having any benefit is probably in the range of 2-5%, and even then usually only for a very brief duration. Dr. REDACTED further testified to relatively new data, that either has been or is about to be published in the journal *Seminars on Oncology*, that even looking at a patient population after progressing on Avastin who received the NovoTTS device, the duration of disease stability or progression free

⁹ Although the disputed device in this case does not fall into the category of a drug or chemotherapy agent, I note that the *European Journal of Cancer* is included in the Medicare list of acceptable peer-reviewed medical literature to be considered when determining a medically accepted indication for the off-label use of drugs or biologicals in an anti-cancer chemotherapeutic regimen. *Medicare Benefit Policy Manual, Pub. 100-02, Ch. 15, §50.4.5.*

interval is significantly longer than any other treatment reported in the literature, making it an appropriate treatment in the setting of the Beneficiary in this case, and, in Dr. REDACTED opinion the best treatment available for the Beneficiary, outside of experimental clinical trials for which Dr. REDACTED indicates the Beneficiary was not eligible and/or are unproven. Dr. REDACTED further testified, anecdotally, that he has used the Device on occasion for his patients, particularly in situations similar to the Beneficiary's situation in this case, and he has found the Device to be of benefit.

Local Coverage Determination L34730, issued by Medicare Contractor NHIC Corp. (responsible for payment of claims under original Medicare Part B), states that "Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary." The LCD cites a review of some 17 studies or articles as sources of information and basis for the LCD decision, with dates from 2007 through 2013, including some of the same studies cited in the Supplier's submitted literature. However, the LCD does not provide any specific analysis of the Contractor's review of these studies or any rationale for the determination that tumor treatment field therapy treatment is not reasonable and necessary for tumor treatment. There is some question as to why this particular LCD was chosen in this case.¹⁰ However, I note that the three other LCDs issued by different DME Medicare Contractors, also state that "Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary." See LCD L34665 issued by CGS Administrators; LCD L34734 issued by Noridian Healthcare Solutions; and, L34738 issued by National Government Services. Mr. Kelly testified that to his knowledge the LCD was written by the four regional DME Medical Directors and their staff, without consult with an advisory committee including neuro-oncologists or neuro-surgeons, resulting in his understanding that the LCDs are currently being reviewed by CMS at the request of the Supplier.

VI. ANALYSIS

I have reviewed the criteria necessary for Medicare coverage of the claimed Device, as such criteria have been established in accordance with the Plan EOC and the Medicare statutory, regulatory, and other guidance provisions pertinent to coverage under Part C of Title XVIII (Medicare Part C). Based thereupon, I have determined that the criteria for coverage have been met. Therefore, the Plan must authorize coverage for the claimed Device for use consistent with physician orders and the Device Supplier's product guidelines. See *NovoTTF-100A System Product Dossier, Description and Use of NovoTTF-100A System*, p. 20.

More specifically, Medicare coverage under the DME benefit requires that the item meet the definition of durable medical equipment, be reasonable and necessary for the treatment of the patient's illness or injury or to improve the functioning of his or her malformed body member as required by Section 1862(a)(1)(A) of Title XVIII (medical necessity), and be for home use. See

¹⁰ Medicare rules require an MA organization to comply with applicable written coverage decisions of Original Medicare contractors (e.g. LCDs) with jurisdiction for claims in the geographic area in which such services are covered under the MA plan. (If an MA plan covers geographic areas encompassing more than one local coverage policy area, the MA organization offering such an MA plan may elect to apply to plan enrollees in all areas uniformly the coverage policy that is the most beneficial to MA enrollees.) See 42 C.F.R. §422.101(b).

CMS Pub. 100-02, Ch. 15, §110 et seq. Sufficient documentation should be submitted to support the claim, including a physician's order and sufficient medical record documentation to support that Medicare criteria, including medical necessity, have been met. *See CMS Pub. 100-08, Ch. 5.*

In this case, there is no question that the claimed NovoTTF-100A System Device, coded pursuant to E0766 (electrical stimulation device used for cancer treatment, includes all accessories, any type) meets the Medicare definition of DME for home use. However, the Plan denied coverage based upon a Local Coverage Determination, which simply states, without explanation, that "Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary." Medicare Regulations at 42 CFR §405.1062 provide that in making coverage determinations ALJs will give substantial deference to policy guidance, including applicable LCDs. However, an ALJ is not required to follow such policy guidance upon providing an explanation in the decision as to why the guidance will not be followed. *See Id.*

In this case, although I have given substantial deference to the LCD, I decline to follow the LCD and instead find that the Device will be considered reasonable and necessary for this beneficiary for the FDA indicated condition as stated in the April 8, 2011 FDA pre-market approval letter issued for the Device.

In declining to follow the pertinent LCD for this beneficiary, I have considered the following criteria, as suggested by Medicare manual guidance: (1) whether the device can be expected to make a meaningful contribution to the treatment of the patient's illness or injury or to the improvement of his or her malformed body member; (2) whether the device can be considered a reasonable treatment, considering expense versus therapeutic benefits, comparative cost of feasible alternatives, and whether the device serves comparative purposes with other equipment or alternatives; (3) whether all features of the device are required for treatment of the Beneficiary's condition; and, (4) the period of time the DME will be considered medically necessary, which is generally based on the physician's estimate of the time that his or her patient will need the equipment. *CMS Pub. 100-02, Ch. 15, §110(c).*

Based upon consideration of the submitted peer reviewed literature and studies and medical testimony, I find that these conditions are met for use of the device for FDA indicated treatments in this beneficiary. I find that the Device as used consistent with FDA indications can be expected to make a meaningful contribution to the treatment of the Beneficiary's recurrent supratentorial glioblastoma multiforme, that the FDA requires that all feasible alternatives have been exhausted prior to use of the Device, that there are no features of the Device not required for treatment, and that the medically necessary duration of treatment can properly be determined by physician orders.

Therefore, I find that the Device will be considered reasonable and necessary for this beneficiary pursuant to the FDA indications for treatment stated in the April 8, 2011 FDA pre-market approval letter, as follows:

This device is indicated for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically – or radiologically – confirmed recurrence in the supratentorial region of the brain after

receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted.

April 8, 2011 FDA Premarket Approval Letter (found at www.fda.gov).

I also find that the request for pre-authorization of use of the Device in this beneficiary is in conformance with the foregoing FDA indications in this case. The medical record and testimony confirm that the Beneficiary suffers from recurrent histologically (July 2013 pathology report) and radiologically (August and October 2014 MRIs) confirmed supratentorial glioblastoma multiforme, following two surgical interventions, two radiation treatments and the use of chemotherapy treatment with Temodar (Temozolomide), as well as, in this case, additional treatment with Avastin. I find that this record further supports the testimony of Dr. Larocca that all such traditional options have been exhausted, and that accordingly FDA criteria are met for treatment with the Device.

Accordingly, the use of the Device pursuant to appropriate physician orders is found to be reasonable and necessary as required for Medicare coverage.

VII. CONCLUSIONS OF LAW

MA plans offered under Medicare Part C must generally provide or pay for medically necessary Original Medicare Part A and Part B covered items and services, though additional optional supplemental coverage may also be offered by an MA plan. *CMS Pub. 100-16, Ch. 4, §§10.2-10.3*. Benefits are disclosed to members through a variety of means, including a Plan Evidence of Coverage which is approved by the Centers for Medicaid & Medicare Services. See 42 C.F.R. §422.11; *CMS Pub. 100-16, Ch. 3*. The Appellant's request for pre-authorization of the NovoTTF-100APlus Transducer Device, HCPCS Code E0766, meets requirements for Medicare coverage because the device is shown to: meet the definition of DME, be reasonable and necessary for the treatment of the Beneficiary's recurrent glioblastoma multiforme, and be for use in the Beneficiary's home. See Sections 1832(a)(1), 1834(a)(13), 1861(n),(s)(6), 1862(a)(1)(A) of Title XVIII 42 C.F.R. §410.38(a); *CMS Pub. 100-02, Ch. 15, §110 et seq.* Accordingly, the Plan shall authorize coverage for treatment of the Beneficiary's recurrent glioblastoma multiforme with the Device pursuant to orders of an oncologist or other qualified physician trained in the use of the Device and consistent with Supplier guidelines.

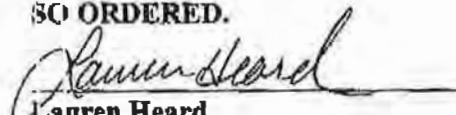
VIII. ORDER

The Plan is **DIRECTED** to process the claim in accordance with this decision.

Date

11/10/14

SO ORDERED.


Lauren Heard
U.S. Administrative Law Judge

Administrative Law Judge Decision

Appellant: **REDACTED**

Appeal No. 1-2669116429

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**UNITED STATES DEPARTMENT
OF
HEALTH AND HUMAN SERVICES
OFFICE OF MEDICARE HEARINGS AND APPEALS
Miami, Florida**

Appeal of:

ALJ Appeal No.: 1-4757777158

Beneficiary:

e

Medicare Part C

HICN:

XXX-XX-XXXX

Before: Lauren Heard

U.S. Administrative Law Judge

ADMINISTRATIVE LAW JUDGE DECISION AND ORDER

I. SUMMARY OF DECISION

After carefully considering the evidence and arguments presented, a **Fully Favorable** decision is entered for the Beneficiary, (“Beneficiary” or “you”) who is also the Appellant. As set forth in more detail herein, the Medicare PLUS Blue Group PPO Medicare Advantage Plan offered by Blue Cross Blue Shield of Michigan, (“Plan”) incorrectly denied coverage for a tumor treatment fields device and specifically treatment with the Optune device (formerly NovoTTF-100A system) coded pursuant to E0766 (“Optune Device”). Therefore, the Beneficiary is entitled to Plan coverage for six months treatment with the Optune Device pursuant to the May 24, 2016 orders of the Beneficiary’s treating physician.

II. PROCEDURAL HISTORY

On May 24, 2016, the Beneficiary’s physician, Dr. MD, prescribed the use of Optune, formerly NovotTTF – 100A System, including up to 40 disposable transducer arrays per month for six months, for a diagnosis of ICD-10 C71.9 (malignant neoplasm of brain, unspecified), Glioblastoma, noting that the Beneficiary was an existing patient already using Optune. *Ex. 2, p. 3.*

The Plan denied a request for prior authorization on initial and redetermination for monthly rental of the Optune plus transducers, coded as durable medical equipment (“DME”) pursuant to HCPCS Code E0766 (Electrical stimulation device used for cancer treatment, includes all accessories, any type). *Ex. 1, pp. 9, 48-49.* As required pursuant to Medicare rules, the Plan forwarded the denial to the Independent Review Entity, (also called the Part C QIC) Maximus Federal Services, who again denied the claim. The QIC found that the Plan did not have to pre-approved the Optune Device because, pursuant to Local Coverage Determination L34823, titled Tumor Treatment Field Therapy (TTFT) (LCD L34823), tumor treatment fields therapy (E0766) will be denied as not reasonable and necessary. *Ex. 1, p. 4.*

On or about July 22, 2016, the Part C QIC received a request for Administrative Law Judge (“ALJ”) hearing, which was forwarded to the Office of Medicare Hearings and Appeals on July 25, 2016. *Ex. 3*. The request was timely and the amount in controversy satisfies the jurisdictional requirement for an ALJ hearing pursuant to Title XVIII of the Social Security Act (the “Act” or “Title XVIII”) Sections 1852(g)(5) and 1869(b)(1)(E).

A telephonic hearing was held on September 29, 2016. The Beneficiary appeared at the hearing as did representatives from the Device Supplier, Novocure, Shannon Fisher, Novocure Case Manager/Head of Territory for the Central Region and Tanya Lane, Novocure Case Manager/Team Lead. On behalf of the Plan, Angela Whetstone, Senior Team Lead, Blue Cross Blue Shield Grievance and Appeals Department, appeared at the hearing.

Exhibits 1 – 9 have been admitted into evidence and considered along with the hearing testimony. Good cause is found for the admission of new documentation, found at Exhibit 9, submitted to the ALJ due to the need for updated documentation concerning the Optune Device efficacy and FDA approval. *See 42 C.F.R. §§405.1018, 1028* (requiring a finding of good cause to admit evidence first submitted at ALJ level of appeal).

III. ISSUES

The issue is whether the Plan must authorize coverage for treatment with the Optune Device coded pursuant to E0766, i.e. is the Device covered and payable by the Plan pursuant to Section 1851 et seq. of Title XVIII (Medicare Part C).

IV. LEGAL FRAMEWORK

The Medicare program, Title XVIII of the Social Security Act (42 U.S.C. §§ 1395 – 1395ccc), is administered through the Centers for Medicare and Medicaid Services, or CMS. Title 42 of the Code of Federal Regulations, (“C.F.R.”), Chapter IV contains implementing regulations. Centers for Medicare and Medicaid Services, (“CMS”) Rulings and Manual Guidance and National and Local Coverage Determinations may also be cited herein, when applicable.¹

I. ALJ Review Authority

Plan determinations are subject to appeals procedures set forth under the Medicare Advantage Program, also known as Medicare Part C.

A. Jurisdiction

An enrollee who receives an adverse Medicare Advantage (“MA”) plan determination, including the MA organization’s refusal to provide or pay for services in whole or part, is entitled to a Reconsideration by the MA organization, and if not thereafter satisfied, to a subsequent Reconsideration to be performed by an Independent Review Entity, or, IRE. *See Section 1852(g) of Title XVIII; 42 C.F.R. §§422.566; 422.576-596*. Enrollees or providers dissatisfied with the IRE’s Reconsideration are entitled to a hearing before the Secretary of the Department of Health and Human Services (“HHS”), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. *See Section 1852(g)(5) of Title XVIII; 42 C.F.R. §§422.600-602*.

¹ Many of the sources cited herein are available at www.cms.gov.

In implementing this statutory directive, the Secretary has delegated her authority to administer the nationwide hearings and appeals system for the Medicare program to the Office of Medicare Hearings and Appeals (“OMHA”). *See* 70 *Fed. Reg.* 36386, 36387 (June 23, 2005); *See also* 42 *C.F.R.* §§422.600-602. The Administrative Law Judges, ALJs, within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*; *See also* 42 *C.F.R.* §422.608. The parties to the ALJ hearing may include the plan enrollee (also referred to herein as the beneficiary or member), an assignee of the enrollee (that is, a physician or other provider who has furnished a service to the enrollee and formally agrees to waive any right to payment from the enrollee for that service), the MA organization (i.e. the Plan), and any other person, provider or entity whose rights may be affected by the hearing as determined by the ALJ or at any lower level of appeal. *See* 42 *C.F.R.* §422.602(c); *See also* 422.574; 422.582(d); 422.592(c).

The request for an ALJ hearing is timely if filed within sixty days after receipt of a Reconsideration issued by the IRE. *See* 42 *C.F.R.* §422.602. To be entitled to an ALJ hearing, a party must meet the minimum amount in controversy requirement of \$100; however, this minimum is subject to increases which are published in the Federal Register. 42 *C.F.R.* §§405.1006; 422.600. The amount in controversy threshold for ALJ hearing requests filed during the year 2016 is \$150. 80 *Fed. Reg.* 57827 (Sep. 25, 2015).

B. Scope of Review

In hearing appeals under Medicare Part C, the ALJ generally applies the same administrative review and hearing processes that are employed in reviewing cases under Original Medicare Parts A and B. 42 *C.F.R.* §422.562(d). Thereunder, the ALJs conduct *de novo* hearings.² *See* 70 *Fed. Reg.* 36386, 36387 (June 23, 2005); 42 *C.F.R.* §405.1000(d). The issues before the ALJ include all the issues brought out in the Plan determination, Plan reconsideration or IRE reconsideration that were not decided entirely in the appellant’s favor. However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, notice will be sent to the appellant and it will be considered at the hearing. *See* 42 *CFR* 405.1032.

All laws, regulations and Centers for Medicare and Medicaid Services (“CMS”) rulings pertaining to the Medicare and Medicaid programs, including, but not limited to Titles XI, XVIII, and XIX of the Social Security Act and applicable implementing regulations are binding on ALJs. 42 *C.F.R.* §405.1063.

The Administrative Law Judge’s, or ALJ’s, application of National Coverage Determinations (“NCDs”),³ written coverage decisions of Medicare contractors, also called Local Coverage Determinations, or LCDs⁴, and CMS manual guidance is also addressed under Medicare law. Section 1871(a)(2) of Title XVIII provides that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare

² In a *de novo* review, the ALJ conducts a new and independent review of the record and is not bound by any previous decision(s) issued in a case.

³ An NCD is a determination by the Secretary of whether a particular item or service is covered nationally. *See* 42 *C.F.R.* §405.1060.

⁴ An LCD is a Original Medicare Part A or B contractor-wide written policy coverage determination as to whether particular items or services are medically reasonable and necessary. *See* 42 *C.F.R.* §400.202.

Administrative Law Judge Decision

Appellant

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program. *Medicare Regulations at 42 C.F.R. 405.1060(4)* provide that an applicable NCD is binding on ALJs. *Medicare Regulations at 42 CFR §405.1062* provide that in making coverage determinations ALJs will give substantial deference to policy guidance including applicable LCDs or CMS program guidance, such as program memoranda and manual instruction. However, an ALJ is not required to follow such policy guidance. An explanation in the decision is required if the ALJ does not follow such policy guidance.

II. Medicare Part C – Medicare Advantage Plan Coverage

A. General Framework for Medicare Part C

Section 1851 et seq. of Title XVIII establishes the Medicare Advantage Program, also referred to as Medicare Part C, which permits eligible individuals to receive Medicare benefits through enrollment in a private health insurance plan, typically referred to as a Medicare Advantage, or MA plan. Medicare Regulations at 42 C.F.R. Part 422 provide rules governing the Medicare Advantage Program. Medicare Managed Care Manual, Pub. 100-16, (“*CMS Pub. 100-16*”) also offers guidance regarding the Medicare Advantage Program. This authority explains that the benefits offered by an MA plan are reviewed and approved by CMS to ensure that Medicare guidelines have been met. *42 C.F.R. §§422.100(f); CMS Pub. 100-16, Ch. 4, §10.2.1*. The plan provides eligible enrollees, at a minimum, basic benefits, which include all medically necessary Medicare covered Part A and Part B services, except hospice services, certain clinical trial services and certain service during inpatient stays during which MA plan enrollment begins or ends. *See Id.; 42 C.F.R. §§422.100(a), (c); 422.101(a)*.⁵ Accordingly,

An MAO [Medicare Advantage Organization] offering an MA plan must provide enrollees in that plan with all Part A and Part B, Original Medicare services, if the enrollee is entitled to benefits under both parts, and Part B services if the enrollee is a grandfathered “Part B only” enrollee. The MAO fulfills its obligation of providing Original Medicare benefits by furnishing the benefits directly, through arrangements, or by paying for the benefits on behalf of enrollees. . . .

Administration of the Medicare program is governed by title XVIII of the Social Security Act (the Act). Under the Medicare program, the scope of benefits available to eligible beneficiaries is prescribed by law and divided into several main parts. Part A is the hospital insurance program and Part B is the voluntary supplementary medical insurance program.

The scope of the benefits under Part A and Part B is defined in the Act. The scopes of Part A and Part B are discussed in sections 1812 and 1832 of the Act, respectively, while section 1861 of the Act lays out the definition of medical and other health services. Specific health care services must fit into one of these benefit categories, and not be otherwise excluded from coverage under the Medicare program (see §1862 for exclusions).

In general, the Act lists categories of items and services covered by Medicare, although Congress occasionally adds specific services to be covered by Medicare. Some categories are defined more broadly than others; for example, the Act includes hospital outpatient services furnished incident to physicians’ services (§1861(s)(2)(B)) but also specifically includes diabetes screening tests (§1861(s)(2)(Y)). The Secretary has the authority to make

⁵ Medicare Part D prescription drug benefits may also be offered through MA organizations in conjunction with their MA plan. *See 42 C.F.R. §422.4(c)*.

determinations about which specific items and services, within categories, may be covered under the Medicare program. Further interpretation is provided in the Code of Federal Regulations and CMS guidance.

In general, Medicare coverage and payment is contingent upon a determination that:

- A service is in a covered benefit category;
- A service is not specifically excluded from Medicare coverage by the Act; and
- The item or service is "reasonable and necessary" for the diagnosis or treatment of an illness or injury or to improve functioning of a malformed body member, or is a covered preventive service.

CMS Pub. 100-16, Ch. 4, §10.2.

In addition to providing Original Medicare benefits, to the extent applicable, the Medicare advantage organization, or MAO, also furnishes, arranges, or pays for supplemental benefits and prescription drug benefits to the extent they are covered under the plan. *CMS Pub. 100-16, Ch. 4, §10.2.1.*

Medicare Regulations at 42 C.F.R. §422.111 state that an MA plan must disclose the benefits offered under a plan, including applicable conditions and limitations, premiums and cost-sharing (such as copayments, deductibles, and coinsurance) and any other conditions associated with receipt or use of benefits to its enrollees. This information may be found in the MA Plan Evidence of Coverage, ("EOC"), which MA plans provide to enrollees upon enrollment, on an annual basis and through the plan's internet web site. These disclosure rules are also discussed in CMS Pub. 100-16, Ch. 3. All such marketing materials used by plan sponsors or their subcontractors must be submitted by the plan sponsor (or its designee) to CMS for review and approval (or acceptance). *See CMS Pub. 100-16, Ch. 3, §30.3.*

In making benefit determinations, the MA organization complies with CMS's national coverage determinations (NCDs), general coverage guidelines included in CMS's Medicare manuals and instructions (unless modified by Federal regulations or related instructions), and applicable written coverage decisions of Original Medicare contractors (e.g. LCDs) with jurisdiction for claims in the geographic area in which such services are covered under the MA plan. (If an MA plan covers geographic areas encompassing more than one local coverage policy area, the MA organization offering such an MA plan may elect to apply to plan enrollees in all areas uniformly the coverage policy that is the most beneficial to MA enrollees.) *See 42 C.F.R. §422.101(b).*

B. Plan Evidence of Coverage (EOC)

Because the Plan discloses its covered benefits in its Evidence of Coverage, or EOC, it is necessary to review that document to determine policy coverage. Your EOC further explains that

- Durable medical equipment and medical supplies – the Plan covers medically necessary items that you purchase or rent from an independent medical supplier for use at home. You must have a prescription or Certificate of Medical Necessity from a Doctor of Medicine (M.D.) or Doctor of Osteopathy (D.O.) to obtain Durable Medical Equipment (DME). *EOC, Chapter 4, Medical Benefits Chart.*
- Your Medicare covered services must be provided according to the coverage guidelines established by Medicare. *EOC, Chapter 4, Section 2.1.*

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- Your services (including medical care, services, supplies, and equipment) *must* be medically necessary. ‘Medically necessary’ means that the services, supplies, or drugs are needed for the prevention, diagnosis, or treatment of your medical condition and meet accepted standards of medical practice. *Id.*

C. Pertinent Original Medicare Coverage Rules

Because Medicare rules provide that your Medicare Part C Medicare advantage plan must include benefits provided under and according to Medicare coverage guidelines established by Original Medicare Parts A and B, it is also instructive to review those guidelines, as established by statute, regulation, NCD, LCD and CMS manual guidance.

Sections 1831 et seq. of Title XVIII establish the Supplementary Medical Insurance Benefits for the Aged and Disabled (Medicare Part B). Section 1832 of Title XVIII and Medicare Regulations at 42 C.F.R. §410.3 establish the scope of benefits that are provided to eligible beneficiaries under the Medicare Part B insurance program, which includes “medical and other health services.” Sections 1832(a)(1), 1861(n),(s)(6) and 1834(a)(13) of Title XVIII and Medicare Regulations at 42 C.F.R. §410.38(a) provide that covered “medical and other health services” under Medicare Part B include, among many other things, the rental or purchase of durable medical equipment (“DME”), if the equipment is used in the patient’s home or in an institution that is used as a home.

Section 1862(a)(1)(A) of Title XVIII provides that “[n]otwithstanding any other provision of the Act, no payment shall be made for any expenses incurred for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” *See also 42 CFR §411.15(k).*

Medicare National Coverage Determinations Manual, Pub. 100-03 (“CMS Pub. 100-03”), Ch. 1, includes National Coverage Determinations. *CMS Pub. 100-03, Ch. 1, §280.1* explains that the term Durable Medical Equipment, or DME, is defined as equipment which:

- Can withstand repeated use; i.e., could normally be rented, and used by successive patients;
- Is primarily and customarily used to serve a medical purpose;
- Generally is not useful to a person in the absence of illness or injury; and
- Is appropriate for use in a patient’s home.

Medicare Benefit Policy Manual, Pub. 100-02 (“CMS Pub. 100-02”), Ch. 15, §110, also provides guidance pertaining to Medicare coverage of DME, and explains that:

Expenses incurred by a beneficiary for the rental or purchases of durable medical equipment (DME) are reimbursable if the following three requirements are met:

- The equipment meets the definition of DME [see above];
- The equipment is necessary and reasonable for the treatment of the patient’s illness or injury or to improve the functioning of his or her malformed body member (§110.1); and
- The equipment is used in the patient’s home.

CMS Pub. 100-02, Ch. 15, §110(c) provides guidance as to the “necessary and reasonable” requirement, and states as follows:

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Although an item may be classified as DME, it may not be covered in every instance. Coverage in a particular case is subject to the requirement that the equipment be necessary and reasonable for treatment of an illness or injury, or to improve the functioning of a malformed body member. These considerations will bar payment for equipment which cannot reasonably be expected to perform a therapeutic function in an individual case or will permit only partial therapeutic function in an individual case or will permit only partial payment when the type of equipment furnished substantially exceeds that required for the treatment of the illness or injury involved.

1. Necessity for the Equipment

Equipment is necessary when it can be expected to make a meaningful contribution to the treatment of the patient's illness or injury or to the improvement of his or her malformed body member. In most cases the physician's prescription for the equipment and other medical information available to the DMERC will be sufficient to establish that the equipment serves this purpose.

2. Reasonableness of the Equipment

Even though an item of DME may serve a useful medical purpose, the DMERC or intermediary must also consider to what extent, if any, it would be reasonable for the Medicare program to pay for the item prescribed. The following considerations should enter into the determination of reasonableness:

1. Would the expense of the item to the program be clearly disproportionate to the therapeutic benefits which could ordinarily be derived from use of the equipment?
2. Is the item substantially more costly than a medically appropriate and realistically feasible alternative pattern of care?
3. Does the item serve essentially the same purpose as equipment already available to the beneficiary?

3. Payment Consistent With What is Necessary and Reasonable

Where a claim is filed for equipment containing features of an aesthetic nature or features of a medical nature which are not required by the patient's condition or where there exists a reasonably feasible and medically appropriate alternative pattern of care which is less costly than the equipment furnished, the amount payable is based on the rate for the equipment or alternative treatment which meets the patient's medical needs.

The acceptance of an assignment binds the supplier-assignee to accept the payment for the medically required equipment or service as the full charge and the supplier-assignee cannot charge the beneficiary the differential attributable to the equipment actually furnished.

4. Establishing the Period of Medical Necessity

Generally, the period of time an item of durable medical equipment will be considered to be medically necessary is based on the physician's estimate of the time that his or her patient will need the equipment. See the Medicare Program Integrity Manual, Chapters 5 and 6, for medical review guidelines.

Local Coverage Determination L34823, titled "Tumor Treatment Field Therapy (TTFT)" adopted by Medicare Contractors CGS Administrators, LLC and Noridian Healthcare Solutions, LLC, ("LCD L34823") states "Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary."

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Medicare Program Integrity Manual, Pub. 100-08 ("CMS Pub. 100-08"), Ch. 5, also provides guidance as to documentation requirements to support that Medicare coverage criteria for items of DME have been met. Chapter 5, Section 5.7 states as follows, in pertinent part:

For any DMEPOS item to be covered by Medicare, the patient's medical record must contain sufficient documentation of the patient's medical condition to substantiate the necessity for the type and quantity of items ordered and for the frequency of use or replacement (if applicable). The information should include the patient's diagnosis and other pertinent information including, but not limited to, duration of the patient's condition, clinical course (worsening or improvement), prognosis, nature and extent of functional limitations, other therapeutic interventions and results, past experience with related items, etc. . . . neither a physician's order nor . . . a supplier prepared statement nor a physician attestation by itself provides sufficient documentation of medical necessity, even though it is signed by the treating physician or supplier. There must be information in the patient's medical record that supports the medical necessity for the item and substantiates the answers on the CMN [certificate of medical necessity] (if applicable) or DIF [DME information form] (if applicable) or information on a supplier prepared statement or physician attestation (if applicable).

V. FINDINGS OF FACT

The medical record

The record as received from the QIC, includes a prescription for the Beneficiary's use of the Optune Device signed on May 24, 2016 by Dr. MD, *Ex. 2, p. 3*, who also signed a letter of medical necessity on August 22, 2016. *Ex. 7, pp. 6-9*.

The prescription indicates that as of May 24, 2016, the Beneficiary was an existing patient already using the Optune Device, and prescribes the use of Optune (formerly NovotTFF-100A System), including up to 40 disposable transducer arrays per month for six months, with a diagnosis of ICD-10 C71.9 (malignant neoplasm of brain, unspecified), Glioblastoma. *Ex. 2, p. 3*.

In his letter of medical necessity, as supported by submitted progress notes, Dr. explains that the Beneficiary is a agnosed with Glioblastoma, after initially presenting in June of 2014 with increasing fatigue, followed by nausea and vomiting and a fall. The Beneficiary underwent a craniotomy on July 8, 2014, followed by chemoradiation with concurrent Temodar (temozolomide) treatment from August 12, 2014 through September 23, 2014. *Ex. 2, p. 10; Ex. 7, p. 6; Hearing Testimony – Lane*.

Thereafter, on October 27, 2014, the Beneficiary was enrolled in the Novocure EF-14 clinical trial using the Optune Device. The Beneficiary continued to use the Optune Device as part of that clinical trial until the spring of 2016 (at least through May 9, 2016 per progress notes), when the clinical trial ended for all trial participants. As reflected in Dr. letter of medical necessity and submitted progress notes, the Beneficiary also completed 12 cycles of adjunct Temodar (temozolomide) through August 28, 2015. *Ex. 2, pp. 5-10; Ex. 7, p. 6; Hearing Testimony – Lane*.⁶

⁶ Ms. Lane testified that adjunct Temodar (temozolomide) chemotherapy treatment continued during the entirety of the Optune clinical trial, through the spring of 2016. *Hearing Testimony – Lane*. However, the submitted medical record and letter of medical necessity confirm that the Beneficiary completed 12 cycles of adjunct Temodar (temozolomide) through August 28, 2015, and that treatment with the Optune Device continued without further chemotherapy treatment thereafter. *See Ex. 2, pp. 5, 17; Ex. 7, p. 6*.

Dr. continues, in his letter of medical necessity, that MRIs taken from February 3, 2015 through July 20, 2015 were stable with no new enhancement, and that MRIs taken from September 14, 2015 through March 7, 2016, also remained stable with no signs of tumor progression. According to Dr. as confirmed by submitted progress notes, the Beneficiary's most recent MRI, taken on May 9, 2016, was also stable. And, the Beneficiary's Karnofsky Performance Scale (KPS) score as of May 9, 2016 remained at 90, indicating a relatively high ability to continue carrying out normal daily activities. *Ex. 2, pp. 5-6, 10-17; Ex. 7, p. 6.*

Ms. Lane testified that the Beneficiary is still using the Optune Device, with no recurrence according to documentation received from physician's office. *Hearing Testimony – Lane.*

Tumor Treating Fields Therapy

Pursuant to an informal benefit category determination issued by the CMS Director of DMEPOS Policy on July 26, 2013, the NovoTTF-100A System (now called Optune) is a non-invasive system used in the patient's home that delivers tumor treating fields therapy to the brain to disrupt rapid cell division exhibited by recurrent Glioblastoma Multiforme (GMB) tumors, comprised of a durable electrical field generator and disposable insulated transducer arrays for use with the generator which meets the Medicare definition of durable medical equipment (DME), and therefore falls into the DME benefit category, in that it: can withstand repeated use; has an expected life of at least three years; is primarily and customarily used to serve a medical purpose; generally is not useful to a person in the absence of an illness or injury; and is appropriate for use in the home. *Ex. 1, p. 39. See also Policy Article A52711* (indicating that tumor field therapy devices are covered under the Medicare DME benefit (Social Security Act §1861(s)(6), so long as other requirements such as reasonable and necessary requirements are met).

The Supplier has submitted documentation confirming that the Optune Device received an initial April 2011 FDA pre-market approval and later October 2015 FDA pre-market approval supplement. Additional studies and literature have been submitted pertaining to the efficacy of tumor treating fields therapy for indications stated in those FDA approvals, including use of the Optune Device for treatment of recurrent Glioblastoma which has not responded to standard therapy (per the April 2011 FDA approval) and for treatment of newly diagnosed Glioblastoma (per the October 2015 FDA approval supplement).

Local Coverage Determination L34823, adopted by Medicare Contractors CGS Administrators, LLC and Noridian Healthcare Solutions, LLC (responsible for payment of claims under original Medicare Part B), and as currently in effect, states that "Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary." The LCD cites a review of some 17 studies or articles as sources of information and basis for the LCD decision, with dates from 2007 through 2013, including some (but not all) of the same studies cited in the Supplier's submitted literature. However, the LCD does not provide any specific analysis of the Contractors' review of these studies or any rationale for the determination that tumor treatment fields therapy treatment is not reasonable and necessary for tumor treatment in this particular case. Moreover, no reference is made in the LCD to the more recent pivotal study and resulting October 2015 FDA pre-market approval supplement allowing the Optune Device to be used for newly diagnosed Glioblastoma.

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Turning more specifically to documentation of the FDA approved indications for the Optune Device (formerly NovoTTF-100A System), pursuant to the April 2011 FDA approval, the

device is indicated for treatment of adult patients (22 years of age and older) with histologically-confirmed glioblastoma multiform, following histologically – or radiologically – confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiations options have been exhausted. *Ex. 1, p. 43.*

On October 5, 2015, the FDA issued a premarket approval supplement for the Optune Device, which provides the following additional indication:

This device is indicated as a treatment for adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme (GBM). Optune with temozolomide is indicated for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy. *Ex. 9.*

An FDA news release, also dated October 5, 2015, confirms that “[f]or newly diagnosed GBM, Optune is not intended to be used as a substitute for standard treatments, but rather, as an adjunct treatment, and should not be used without a physician’s supervision.” *Ex. 9.* This FDA news release indicates that in the clinical study used to support the expanded indication, patients treated with the device and the chemotherapy drug Temozolomide lived on average three months longer than those treated with the drug alone. The FDA confirms that while Optune was initially approved by the FDA to treat patients with Glioblastoma that recurred or progressed after chemotherapy, with this expanded indication, Optune can be used as part of a standard treatment for Glioblastoma before the disease progresses. *Ex. 9.*

The Optune (NOVOTTF-100A System) Instructions for Use booklet confirms the above FDA indications for use, and also summarizes the results of the pivotal clinical study upon which the FDA indication for use of the device with newly diagnosed GBM is based. This study demonstrates that for newly diagnosed GBM, Optune/Temozolomide extends progression free and overall survival significantly compared to patients receiving Temozolomide alone. The study also demonstrates no significant increase in adverse events when Optune treatment was added to Temozolomide. The only common device related adverse event was skin irritation. *Ex. 2, pp. 19-41; See also Optune Clinical Dossier, Ex. 2, pp. 141-164.*

The submitted medical literature from the year 2015 confirms the results of this pivotal study. A 2015 article, titled “An Evidence-Based Review of Alternative Electric Fields Therapy for Malignant Gliomas,” Wong, Lok and Swanson, as published in “Current Treatment Options in Oncology (2015), confirms that pursuant to the phase III clinical trial for subjects with newly diagnosed Glioblastoma, a pre-specified interim analysis of the first 315 subjects after a minimum follow-up of 18 months showed a median progression free survival of 7.1 versus 4.0 months, and median overall survival of 19.6 months versus 16.6 months, for those receiving tumor treatment fields therapy with Temozolomide versus those treated with Temozolomide alone. This article also confirms that there were similar adverse events between the two groups with the exception of

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increased scalp reactions for those receiving tumor treatment fields therapy with Temozolomide. *Ex. 2, pp. 47-57*. As reported in the Journal of American Medical Association (JAMA), this study showed that the addition of tumor treatment fields “to maintenance temozolomide chemotherapy significantly prolonged both progression-free and overall survival.” *See Ex. 2, pp. 165-174 and Ex. 9 (Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma, A Randomized Clinical Trial,* Stupp, R., Tallibert S, et al., JAMA, 2015:314(23):2535-2543).

Moreover, based upon the above indicated result, “An independent data and safety monitoring committee review of the interim data determined that the predefined improvement in PFS [progression free survival] and OS [overall survival] had been met and recommended termination of the study. Following FDA approval of the termination, the study was closed to recruitment and patients in the control group were allowed to crossover and receive Optune. . . . Follow-up for all patients continues: final analysis data are not expected before the end of 2016.” *Ex. 2, p. 154 (Optune Clinical Dossier)*.

VI. ANALYSIS

I have reviewed the criteria necessary for Medicare coverage of the claimed Optune Device, as such criteria have been established in accordance with the Plan EOC and the Medicare statutory, regulatory, and other guidance provisions pertinent to coverage under Part C of Title XVIII (Medicare Part C). Based thereupon, I have determined that the criteria for coverage have been met. Therefore, the Plan must authorize coverage for six months use of the Optune Device as set forth in the May 24, 2016 physician orders.

More specifically, Medicare coverage under the DME benefit requires that the item meet the definition of durable medical equipment, be reasonable and necessary for the treatment of the patient’s illness or injury or to improve the functioning of his or her malformed body member as required by Section 1862(a)(1)(A) of Title XVIII (medical necessity), and be for home use. *See CMS Pub. 100-02, Ch. 15, §110 et seq.* Sufficient documentation should be submitted to support the claim, including a physician’s order and sufficient medical record documentation to support that Medicare criteria, including medical necessity, have been met. *See CMS Pub. 100-08, Ch. 5.*

There is no question that the claimed Optune Device, coded pursuant to E0766 (electrical stimulation device used for cancer treatment, includes all accessories, any type) meets the Medicare definition of DME for home use. However, the Plan denied coverage based upon a Local Coverage Determination, which simply states, without explanation, that “Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.” Medicare Regulations at 42 CFR §405.1062 provide that in making coverage determinations ALJs will give substantial deference to policy guidance, including applicable LCDs. However, an ALJ is not required to follow such policy guidance upon providing an explanation in the decision as to why the guidance will not be followed. *See Id.*

In this case, I decline to follow the LCD and instead find that the Optune Device will be considered reasonable and necessary for this Beneficiary. In declining to follow the pertinent LCD, I have considered the following criteria, as suggested by Medicare manual guidance: (1) whether the device can be expected to make a meaningful contribution to the treatment of the

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patient's illness or injury or to the improvement of his or her malformed body member; (2) whether the device can be considered a reasonable treatment, considering expense versus therapeutic benefits, comparative cost of feasible alternatives, and whether the device serves the same purpose as other available equipment or alternatives; (3) whether all features of the device are required for treatment of the Beneficiary's condition; and, (4) the period of time the DME will be considered medically necessary, which is generally based on the physician's estimate of the time that his or her patient will need the equipment. *CMS Pub. 100-02, Ch. 15, §110(c)*.

Based upon consideration of the submitted literature, studies, medical record and testimony (see letter of medical necessity), I find that these conditions are met when the Optune Device is used in a manner consistent with above cited FDA approved indications. I find that the use of the Optune Device for an FDA approved indication can be expected to make a meaningful contribution to the treatment of the Beneficiary's Glioblastoma multiforme. Moreover, such use of the Optune Device has been shown to improve survival rates over other available therapies. I also find that there are no features of the Optune Device not required for treatment. And, the medically necessary duration of treatment can properly be determined by physician orders for an additional six months use of the Optune Device in this case.

I also find that the pertinent FDA indication for the Optune Device which is at issue in this case can be found in the October 5, 2015 FDA pre-market approval supplement, which states:

Optune with temozolomide is indicated for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy.

More specifically, the request for authorization of use of the Optune Device in this case is in conformance with the foregoing FDA indication. The record supports that the Beneficiary was identified with newly diagnosed Glioblastoma, and that following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy, the Beneficiary began a course of Optune Device therapy with maintenance Temozolomide (12 cycles of Temozolomide through August 28, 2015).⁷ And, as noted above, adding tumor treatment fields to maintenance Temozolomide chemotherapy has been shown to significantly prolong both progression-free and overall survival. *See Ex. 9 (Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma, A Randomized Clinical Trial)*. Moreover, in this case, the Beneficiary's Glioblastoma has remained stable since onset of the use of the Optune Device by the Beneficiary, who was a participant in the very trial upon which the October 5, 2015 FDE pre-market approval supplement relied. This further suggests that treatment with the Optune Device has been and will continue to be beneficial to this Beneficiary. Therefore, continued use of the Optune Device is found to be reasonable and necessary for the

⁷ I interpret the FDA indication for use of Optune "with Temozolomide" to require a standard course of maintenance Temozolomide, such as has been provided in this case, in addition to the use of the Optune Device. Pursuant to FDA label indications, Temodar (temozolomide) is indicated for the treatment of adult patients with newly diagnosed glioblastoma multiforme (GBM) concomitantly with radiotherapy and then as maintenance treatment for six cycles. *See www.fda.gov* (Temodar Highlights of Prescribing Information/Full Prescribing information). In this case, maintenance Temodar (temozolomide) therapy is documented as having already been provided for twelve cycles in conjunction with the Optune Device.

treatment of the Beneficiary's condition.

Based on the foregoing, the Optune Device is covered by Medicare, and consequently, by the Plan in order to treat the Beneficiary's condition under the Plan's durable medical equipment (DME) benefit.

VII. CONCLUSIONS OF LAW

MA plans offered under Medicare Part C must generally provide or pay for medically necessary Original Medicare Part A and Part B covered items and services, though additional optional supplemental coverage may also be offered by an MA plan. *CMS Pub. 100-16, Ch. 4, §§10.2-10.3*. Benefits are disclosed to members through a variety of means, including a Plan Evidence of Coverage which is approved by the Centers for Medicaid & Medicare Services. *See 42 C.F.R. §422.11; CMS Pub. 100-16, Ch. 3*. The Appellant's request for pre-authorization for six months use of the Optune Device, HCPCS Code E0766, meets requirements for Medicare coverage because the device is shown to: meet the definition of durable medical equipment, be reasonable and necessary for the treatment of the Beneficiary's glioblastoma multiforme, and be for use in the Beneficiary's home. *See Sections 1832(a)(1), 1834(a)(13), 1861(n),(s)(6), 1862(a)(1)(A) of Title XVIII 42 C.F.R. §410.38(a); CMS Pub. 100-02, Ch. 15, §110 et seq.* Accordingly, the Plan shall authorize coverage for six months of treatment with the Optune Device pursuant to the May 24, 2016 orders of the Beneficiary's prescribing physician, Dr.

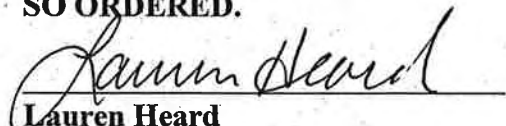
VIII. ORDER

The Plan is **DIRECTED** to process the claim in accordance with this decision.

OCT 18 2016

Date

SO ORDERED.


Lauren Heard
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City, Missouri

Appeal of:

OMHA Appeal No.: **1-6993171990**

Enrollee:

Medicare: **Part C**

HICN: *******2305A**

Before: **Andrew Henningfeld**
Administrative Law Judge

DECISION

Based upon the evidence and arguments of record, an **FULLY FAVORABLE** decision is entered for the Enrollee.

PROCEDURAL HISTORY

The Enrollee, is enrolled in a Medicare Plus Blue Group PPO Medicare advantage (MA) plan. She sought to have the Plan pre-approve coverage for an Optune tumor treatment field therapy (E0766). The Plan denied coverage. The claim was then denied at the prior levels of appeal, including at reconsideration by a qualified independent contractor (QIC). The Enrollee, timely filed a request for an administrative law judge (ALJ) hearing. The Enrollee being a proper party and the amount in controversy being met, a hearing occurred on January 29, 2018. The record is complete and this matter is ready for a decision.

ISSUE

Is the Enrollee entitled to Optune tumor treatment field therapy services under the Medicare Part C plan?

FINDINGS OF FACT

The Enrollee is a 69-year-old female enrolled in a Medicare Plus Blue Group PPO MA plan. The Enrollee was hospitalized in May of 2017, where diagnostic imaging revealed she suffered from a large mass in her right frontal lobe. She underwent a right-frontal craniotomy, which pathology ultimately revealed a grade IV glioblastoma, which is a malignant tumor in the brain. She was recommended for radiation therapy and concurrent Optune treatment, which her neurologist prescribed on September 5, 2017. On November 2, 2017, a neurologist with the Henry Ford Neuroscience Institute reviewed the Enrollee's medical records and drafted a letter highlighting the Enrollee's need for the Optune treatment. This letter supports the conclusion of the Enrollee's physician in prescribing the treatment in this specific case.

[Exh. 2, p. 1-175; Exh. 3, pp. 1-196; Testimony].

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

A party dissatisfied with an IRE's reconsideration determination may request an ALJ hearing. The party must file a request for an ALJ hearing within sixty-five calendar days of the date on the IRE's reconsideration notice, and the requisite amount in controversy requirement must be met. 42 C.F.R. §§ 423.1970, 423.1972, 423.2000, and 423.2002.

B. Scope of Review

The issues before an ALJ include all the issues brought out in the coverage determination, redetermination, or reconsideration that were not decided entirely in an enrollee's favor. 42 C.F.R. § 423.2032(a).

C. Standard of Review

An ALJ conducts a de novo review and issues a decision based on the hearing record. 42 C.F.R. § 423.2000(d). Further, in addition to other binding authorities, an ALJ is governed by the Administrative Procedure Act (APA). 5 U.S.C. §§ 551 to 559 and 3105.

II. Principles of Law

A. The Statutes and Regulations

The Medicare Advantage program, known as Medicare Part C, provides that a MA organization offering a MA plan must provide enrollees, at a minimum, with all basic Medicare-covered services by furnishing the benefits directly or through arrangements, or by paying for the benefits. Basic benefits are benefits defined as "all Medicare covered services, except hospice services." Mandatory supplemental benefits are defined as "services not covered by Medicare that an MA enrollee must purchase as part of an MA plan that are paid for in full, directly by (or on behalf of) Medicare enrollees, in the form of premiums or cost sharing. Optional supplemental benefits are defined as "health services not covered by Medicare that are purchased at the option of the MA enrollee and paid for in full, directly by (or on behalf of) the Medicare enrollee, in the form of premiums or cost sharing. These services may be grouped or offered individually." Social Security Act § 1852(a); 42 CFR § 422.100.

B. Policy and Guidance

When determining benefits coverage and eligibility, ALJs must give substantial deference to applicable policy guidance issued by the Centers for Medicare and Medicaid Services (CMS). 42 C.F.R. § 423.2062.

Analysis

While MA Plans are required to follow local coverage policies, the regulations provide that ALJs are not bound by such policies. 42 C.F.R. § 405.1062(a). Nevertheless, the regulations direct ALJs and the Council to "give substantial deference to these policies if they are applicable to a particular case." The regulations permit an ALJ to decline to follow a local coverage policy in an individual case. 42 C.F.R. § 405.1062(b). The contractor with jurisdiction over the Enrollee's geographical area issued local coverage determination (LCD) L34823. The LCD is entitled "Tumor Treatment Field Therapy (TTFT)" and states that such treatment, billed under HCPCS code E0766, "will be denied as not reasonable and necessary." However, the LCD does not include a list of sources or information on which the determination was based. Other LCDs that address this procedure reference sources related to the use of TTFT for recurrent glioblastoma, not newly discovered glioblastoma. Here, LCD L34823 makes no distinction between recurrent glioblastoma or newly discovered glioblastoma, and the lack of sources or information on which the determination was based makes it unascertainable.

The contractor also issued an accompanying Policy Article, now identified as A52711, which provides "non-medical necessity coverage and payment rules." The article explains that "Code E0766 describes devices that generate electromagnetic fields utilized in the treatment of cancer. The electromagnetic energy generated is transmitted to the body by means of surface electrodes or transducers." The article further states that "[TTFT] devices are covered under the Durable Medical Equipment benefit (Social Security Act § 1861(s)(6)).

Optune is an innovative approach to cancer treatment, using tumor treating fields (TTFields) to interfere with the division of malignant cells. TTFields therapy is a locally or regionally delivered treatment that uses alternating electronic fields to disrupt the rapid cell division exhibited by cancer cells. Optune received pre-market approval by the Food and Drug Administration (FDA) for recurrent glioblastoma in April of 2011 following positive results of a controlled trial. In 2015, Optune received pre-market approval by the FDA for newly diagnosed glioblastoma in combination with temozolomide after standard surgical resection and radiation therapy. The FDA approval helps show that the device is safe, and not experimental or investigational.

Enrollee submitted additional and relevant material in support of her appeal such as the article from the Journal of the American Medical Association (JAMA) titled Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide Vs. Temozolomide Alone for Glioblastoma – A Randomized Clinical Trial. The article describes the superior results in progression free survival as well as overall survival of glioblastoma patients using TTFields. This trial shows that the Optune device was safe, non-investigational and effective. And, this trial shows that the Optune device was appropriate for this individual Enrollee's needs, specifically the treatment of newly discovered glioblastoma.

Additional material submitted by the Enrollee shows the use of TTFT is generally accepted by the medical community. In the 2016 version of the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology Central Nervous System Cancers guidelines, alternating electric field therapy is a treatment option suggested for glioblastoma. This suggestion was found in a treatment guideline from a national cancer organization, not evidence based on an individual physician treating a single patient in a clinical setting. Furthermore, the

MA plan's representative testified at the hearing that private insurance agreements generally cover Optune tumor treatment field therapy. In other words, if the Enrollee had purchased her insurance on the private market and not through a sponsored MA plan, the Optune therapy treatment would likely be covered.¹

Considering the evidence and arguments in this case, the record demonstrates that, in this specific case, the Optune tumor treatment field therapy sought by the Enrollee should be approved. Specifically, the applicable LCD L38423 provides a conclusory statement that the treatment is not allowed without any sources or information on which the determination was based. Enrollee submitted supporting documentation, such as the aforementioned journal article and clinical practice guidelines, showing the positive progression free survival and overall survival rate. This Enrollee had no feasible alternative pattern of care available to her to halt the progression of her disease and her physician prescribed this treatment as the best and only course of action. The November 2, 2017 independent neurologist review and letter further support the Enrollee's need for the Optune treatment in this specific case. The letter concludes the use of Optune treatment, as prescribed by her physician, is medically necessary in this specific case. Based on the Enrollee's condition, her limited treatment options, and positive data for Optune tumor treatment field therapy, the Enrollee should receive the Optune treatment she is requesting.

CONCLUSIONS OF LAW


The MA plan is required to cover the Optune tumor treatment field therapy (E0766) at issue in this appeal. The Optune tumor treatment field therapy (E0766) is medically reasonable and necessary considering the Enrollee's condition. Time is of the essence given the nature of the disease at issue.

ORDER

The Medicare Part C plan sponsor is directed to process the claim in accordance with this decision.

SO ORDERED

Dated: FEB 01 2018


Andrew Henningfeld
Administrative Law Judge

¹ See <https://www.businesswire.com/news/home/20160217005294/en/Anthem-Issues-Positive-Coverage-Decision-Optune-Newly> and <https://www.businesswire.com/news/home/20160303005441/en/Humana-Issues-Positive-Coverage-Decision-Optune>



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri

Appeal of:	ALJ Appeal No.: 1-7901426401
Beneficiary:	Medicare Part: B
HICN:	Before: Andrew Henningfeld Administrative Law Judge

DECISION

Based upon the evidence and arguments of record, a FULLY FAVORABLE decision is entered for the appellant.

PROCEDURAL HISTORY

Mr. [redacted] submitted a claim seeking Medicare Part B payment for the Optune device, previously known as the NovoTTF-100A system (TTFT device)¹ Electric Field Generator device and accessories provided to the beneficiary on multiple dates of service. Following an unfavorable initial determination, redetermination, and reconsideration, Mr. [redacted] timely filed a written request for an administrative law judge (ALJ) hearing. Mr. [redacted] being a proper party and the amount in controversy being met, a hearing was held on October 25, 2018. Appearing at the hearing by phone was Ms. Debra Parrish, the beneficiary's representative, and Ms. Julie Miles, a representative for Novocure. The record is complete and this matter is ready for a decision.

ISSUES

Does Medicare coverage exist for the durable medical equipment, prosthetics, orthotics, and supplies (DMEPOS) at issue? If not, where does financial liability lie?

FINDINGS OF FACT

In the current case, Mr. [redacted] is a 76-year-old male who was diagnosed in April of 2017 with a brain tumor, specifically a "Glioblastoma Multiforme (GBM)." On July 1, 2017, Mr. [redacted]

¹ TTFT stands for tumor treatment field therapy.

underwent a resection of the tumor. Pathology confirmed GBM. Mr. [redacted] then underwent numerous sessions of chemo-radiation, both with and without Temozolomide, which concluded on October 12, 2017. Mr. [redacted] physician signed a prescription and order form for the TTFT device and related supplies on October 5, 2017. The physician signed the order indicating the belief that the TTFT device and accessories/supplies was medically necessary for a six month period. In November, 2017, Mr. [redacted] began treatment with both adjuvant temozolomide, and the TTFT device.

No medical documentation for the dates of service at issue exists in the record; however an Optune Usage Report lists that from November 6, 2017 to January 6, 2018, Mr. [redacted] had a usage compliance rate of 88%. In May of 2018, Mr. [redacted] had a face to face examination with his physician. The physician noted that Mr. [redacted] compliance rate with the TTFT device was approximately 84%. On June 28, 2018, the Mr. [redacted] had another face-to-face evaluation with his physician. The physician noted that the beneficiary was neurologically stable, and was noted to be concurrently taking temozolomide chemotherapy.

No other medical documentation pertinent to the dates of service at issue exists in the record. The record does not contain an Advanced Beneficiary Notice ("ABN"). Both the qualified independent contractor (QIC) and Medicare contractor determined that the beneficiary, Mr. [redacted] was not liable for the cost of the DMEPOS at issue.

(Ex. 2, pp. 1-149; Exh. 4; Exh. 5; Hearing testimony).

LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

A party dissatisfied with a QIC's reconsideration may request an ALJ hearing. The party must file a written request for an ALJ hearing within sixty-five calendar days of the date on the QIC's reconsideration notice, and the requisite amount in controversy requirement must be met. 42 C.F.R. §§ 405.1000(a), 405.1002, and 405.1006.

B. Scope of Review

The issues before an ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in a party's favor. Here, the term "party" does not include a representative of CMS or one of its contractors that may be participating in the hearing. 42 C.F.R. § 405.1032(a).

C. Standard of Review

An ALJ conducts a de novo review and issues a decision based on the hearing record. 42 C.F.R. § 405.1000(d). Further, in addition to other binding authorities, an ALJ is governed by the Administrative Procedure Act (APA). 5 U.S.C. §§ 551 to 559 and 3105.

II. Principles of Law

A. Statutes & Regulations

The statutory authority for the Medicare program is found in Title XVIII of the Act. 42 U.S.C. § 1395 *et seq.* The Medicare program is divided in multiple parts. Medicare Part B is a voluntary insurance program that provides medical insurance benefits to “aged and disabled individuals” for services not covered under Medicare Part A (or Part D). Act § 1831. The individual must elect to enroll in the program. *Id.* The program is financed through contributions appropriated by the Federal Government in addition to premium payments. *Id.* The Secretary of the Department of Health and Human Services has the authority to promulgate regulations which define or clarify the provisions of the Act. 42 C.F.R. § 410 *et seq.*

Section 1832 of the Act establishes the scope of benefits that are provided to an eligible beneficiary under Medicare Part B. *See also* 42 CFR §§ 410.3 and 410.10. Section 1832(a)(2)(B) of the Act indicates an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with a provider. Section 1861(s)(6) of the Act defines the term “medical and other health services” to include durable medical equipment. *See also* 42 CFR §410.36(a)(3).

Medicare coverage for DME is determined in one of three ways. The claim must be decided consistent with an applicable “National Coverage Determination” (NCD).

Act § 1869(c)(3)(B)(ii)(I). If there is no applicable NCD, the decision maker is required to consider, though is not bound, by the Local Coverage Determination (“LCD”) for the geographical area at issue. Act § 1869(c)(3)(B)(ii)(II). If there is no NCD or LCD addressing the matter, the decision maker is required to decide the matter “based on applicable information, including clinical experience and medical, technical, and scientific evidence.”

Act § 1869(c)(3)(B)(ii)(III); *see also* 68 Fed. Reg. 63693.

The regulations define durable medical equipment as follows:

Equipment, furnished by a supplier or a home health agency that:

- 1) Can stand repeated use.
- 2) Effective with respect to items classified as DME after January 1, 2012, has an expected life of at least 3 years.
- 3) Is primarily and customarily used to serve a medical purpose.
- 4) Generally is not useful to an individual in the absence of an illness or injury.
- 5) Is appropriate for use in the home.

42 CFR § 414.202.

Section 1834 of the Act defines the rules for payment of durable medical equipment. *See also* 42 C.F.R. §§ 410.38(g) and 414.210.

Medicare may not make a payment under Part A or Part B for anything which is not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. Act § 1862(a)(1)(A); *see also* 42 C.F.R. §§ 411.15(k) and 414.200 *et seq.* A provider or supplier is responsible for providing sufficient documentation to support the services were medically necessary, the services were provided as bill, and that payment is due. Act §§ 1833(e); *see also* 42 C.F.R. § 424.5(a)(6).

In the event the services are found to be “not medically reasonable and necessary” or “custodial in nature” under Section 1862(a)(1) or (9) of the Act, Section 1879 of the Act provides for limitation on liability for Medicare payments. The regulations address how to determine if the beneficiary or provider/supplier had the requisite degree of knowledge to make them liable under Section 1879 of the Act. 42 C.F.R. § 411.400 *et seq.*; *see also HCFA Ruling 95-1.* If a beneficiary has no knowledge that the services would not be covered, but the provider/supplier of the services did, then the provider/supplier is liable and cannot seek or retain payment made by or on behalf of a beneficiary. 42 C.F.R. § 411.404. In general, the existence of a notice, manual, or community medical standard is sufficient to constitute finding the provider/supplier had notice. 42 C.F.R. § 411.406.

B. Policy and Guidance

Unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. Act § 1871(a)(2); *see also* 42 C.F.R. § 405.1060. An NCD is the Secretary’s determination on Medicare coverage for a particular item or services applied nationally. 42 C.F.R. § 405.1060(a). An ALJ is bound by the NCD and required to ensure the NCD is applied correctly when applicable. 42 C.F.R. § 405.1060(a), (b).

The Secretary has not issued an NCD specifically addressing the DME, or the related supplies, at issue in this case. CMS, *Medicare National Coverage Determinations (Internet-Only Manual Publ’n 100-03)*, ch. 1. *See* NCD § 280.1 *et seq.* regarding DME coverage in general.

CMS and its contractors are permitted to issue policy guidance describing criteria for coverage and payment of selected items and services. 42 C.F.R. § 405.1062. This guidance is located in Medicare’s manuals and local coverage determinations (“LCD”). An ALJ is not bound by the policies outlined in a manual or LCD but is required to give the guidance substantial deference when applicable. 42 C.F.R. § 405.1062(a). An ALJ may decline to follow the guidance but must explicitly explain the reason(s) why. 42 C.F.R. § 405.1062(b). The ALJ’s decision not to follow the policy applies only to the specific claim being considered and has no precedential effect on other claims. *Id.*

CMS and CGS Administrators have published a LCD addressing the DME and related supplies as of the date(s) of service at issue. According to LCD L34823 (Revised January 1, 2017), tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. The LCD does not make a distinction between recurrent or newly-diagnosed GBM. Additionally, under revision history, a note from March 29, 2018 states: “At this time, 21st Century Cures Act will

apply to new and revised LCD's that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and therefore not all the fields included on the LCD are applicable as noted in this policy." However, an earlier revision of this LCD (Revised July 1, 2016) lists 16 sources of information as the basis for decision; the earlier version of the LCD also states that TTFT will be denied as not reasonable and necessary.

ANALYSIS

The overall issue with regards to the current case is whether the TTFT device is medically reasonable and necessary in general for the treatment of newly diagnosed GBM, as opposed to recurrent. Mr. [redacted] representative has indicated that the ALJ should not give deference to the LCD listed above because: LCD L34823 does not provide a summary of the evidence considered and a rationale for the determination as required by the 21st Century Cures Act; and the LCD is currently the subject of a reconsideration request related to whether the LCD applies to newly-diagnosed or recurrent GBM. These arguments are persuasive.

Mr. [redacted] representative first states that because the LCD fails to provide a summary of the evidence considered and a rationale for the determination, as required in the 21st Century Cures Act. The LCD itself partially addresses the issue by stating [the 21st Century Cures Act] "will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination..." This means that the 21st Century Cures Act does not apply to the January 1, 2017 revision because the revision does not further restrict coverage determination. The previous version of the LCD (July 1, 2016), cites sixteen sources utilized as a basis for the decision. However, as noted throughout Mr. [redacted] brief, the citations listed in the previous versions of the LCD only pertain to studies performed on recurrent GBM, as opposed to newly diagnosed GBM. Thus, the citations the LCD relies upon are not pertinent to the current case.

The representative's second argument is that because the LCD is currently the subject of a reconsideration request related to whether the LCD applies to newly-diagnosed or recurrent GBM, the LCD should not be given deference in this case. This is persuasive. In the August 7, 2018 letter referenced by the representative, the DME MAC Medical Directors states that the request to reconsider coverage for newly-diagnosed GBM was a valid one. As mentioned above, the LCD does not make a distinction between recurrent or newly-diagnosed GBM; it flatly states that TTFT therapy will be denied as not reasonable and necessary. The fact that the request for reconsideration was determined to be valid implies that the LCD as written only applies to recurrent GBM, not newly diagnosed GBM. While an ALJ is required to give substantial deference to LCDs, it is persuasive that the LCD as written does not fully address the medical literature or apply to newly diagnosed GBM.

The medical literature as it relates to newly diagnosed GBM is quite compelling. For example, the National Comprehensive Cancer Network (NCCN) gave a level one recommendation for the TTFT device for treatment of newly-diagnosed GBM. As noted by the Appellant's representative, this means that "a consensus exists among the experts based on the highest levels of evidence, that the treatment is recommended." Moreover, one of the phase III studies needed to be halted midway due to ethical considerations: the experimental group was doing so well that

the experimenters believed it would be unethical to not provide the treatment to the control group. Numerous other studies described in the Appellant's brief indicate an effective treatment for newly diagnosed GBM that is persuasive in the absence of an LCD that directly relates to the issue at hand.²

Additionally, the medical documentation provided establishes medical necessity. The Optune device's product dossier, medical literature, and FDA approvals indicate six separate requirements. The six requirements are as follows:

- 1) the individual must be at least 22 years old;
- 2) the individual's medical history includes a diagnosis of GBM;
- 3) there is histological or radiological evidence of GBM in the supratentorial region of the brain after the individual received chemotherapy;
- 4) the individual is not a candidate for further surgery or radiation; and
- 5) the TTFT is being used as a monotherapy in conjunction with temozolomide chemotherapy.
- 6) the individual utilizes usage compliance of over 75%

In the current case, all six requirements have been met. As mentioned above, on October 5, 2017, Mr. _____ physician signed a prescription for the TTFT device, lasting six months. Mr. _____ had been newly diagnosed with GBM, and the location of the GBM was in the required region. During that timeframe, Mr. _____ was placed on a regimen of chemotherapy, which he received both before and after being placed on the TTFT device treatment. In the only face-to-face evaluation included in the record, Mr. _____ was reported to be concurrently taking temozolomide chemotherapy with the TTFT device. This implies that Mr. _____ was receiving the temozolomide chemotherapy regimen during the date of service at issue. Additionally, usage statistic provided in the record make it clear that Mr. _____ usage compliance was over 75%. Because the coverage requirements for the TTFT device have been met, the TTFT device is covered by Medicare.

CONCLUSIONS OF LAW

Based upon a de novo review of the evidence and arguments presented, the following conclusions of law are made.

The record shows the DMEPOS at issue does satisfy the applicable Medicare coverage criteria. The DMEPOS at issue was reasonable and necessary. It is therefore covered under Medicare Part B.

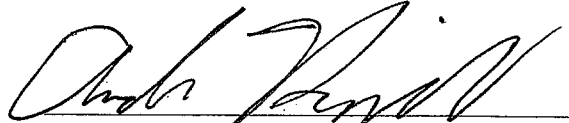
² See Exh. 4 in the case file

ORDER

The Medicare contractor is directed to process the claim in accordance with this decision.

SO ORDERED.

Dated: DEC 19 2018



Andrew Henningfeld
Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City, Missouri

Appeal of: **NOVOCURE INC.**

OMHA Appeal No.: **1-2698137175**

Beneficiary: _____

Medicare: **Part B**

Medicare No.: *******6396A**

Before: **Andrew Henningfeld**
Administrative Law Judge

DECISION

Based upon the evidence and arguments of record, a FULLY FAVORABLE decision is entered for the appellant.

PROCEDURAL HISTORY

Appellant submitted a claim seeking Medicare Part B payment for NovoTTF-100A system (TTFT device)¹ Electric Field Generator accessories provided to the beneficiary. Following an unfavorable initial determination, redetermination, and reconsideration on the second claim, appellant timely filed a written request for an administrative law judge (ALJ) hearing. Appellant being a proper party and the amount in controversy being met, a hearing was held. The record is complete and this matter is ready for a decision.

ISSUES

Does Medicare coverage exist for the durable medical equipment, prosthetics, orthotics, and supplies (DMEPOS) at issue? If not, where does financial liability lie?

FINDINGS OF FACT

The Food and Drug Administration ("FDA") approved the appellant's Pre-Market Approval ("PMA") application for the TTFT device on April 8, 2011. The letter states:

This device is indicated for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically- or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a

¹ TTFT stands for tumor treatment field therapy.

monotherapy, and is intended as an alternative to standard medical therapy for GB after surgical and radiation options have been exhausted.

The National Comprehensive Cancer Network (“NCCN”) updated its guidelines addressing nervous system cancers in late 2012.² The NCCN indicated a physician should “consider alternating electric field therapy (for glioblastoma) (Category 2B).”³ (Journal of National Comprehensive Cancer Network, *Central Nervous Systems Cancers*, Vol. 11 No. 9, p. 1120 (Sept. 2013)).⁴

In the current case, the beneficiary is a 65-year-old female, diagnosed with a brain tumor, specifically a “Recurrent Glioblastoma Multiforme of the Parietal (GBM)” (ICD-9 diagnosis code 191.3). Hearing testimony confirmed that the location of the GBM was in the supratentorial region. The beneficiary initially underwent a right temporal resection on June 19, 2012. Pathology confirmed GBM. The beneficiary then underwent numerous sessions of chemoradiation. The beneficiary’s physician signed a prescription and order form for the TTFT device and related supplies on July 31, 2013 with treatment starting on August 12, 2013 and lasting six months. The physician signed the order indicating the belief that the TTF device and accessories/supplies was medically necessary for a six month period. On August 12, 2013, the beneficiary began treatment with the TTFT device.

On August 12, 2013, the beneficiary had an office visit evaluation with her physician. The office visit notes indicate the beneficiary was starting her NovoTTF treatment at that time. The record indicates the physician and beneficiary were aware that NovoTTF must be used as a monotherapy. And, the notes specifically indicate the beneficiary’s last Avastin chemotherapy regimen occurred on July 2, 2013.

On September 11, 2013, the beneficiary had an office visit evaluation with her physician. The medical record indicates she wore her Novocure device 14-18 hours per day, and her usage compliance rate was documented at 84%. There is no indication in the record that the beneficiary was on a chemotherapy regimen at that time.

On November 6, 2013, the beneficiary had an office visit evaluation with her physician. Her usage compliance rate was documented at 88%. The evaluation does not indicate that she was receiving Avastin or temozolomide treatment at the same time she was receiving TTFT treatment.

(Ex. 2, pp. 1-230); Hearing testimony).

² See Journal of the National Comprehensive Cancer Network, at <http://www.jnccn.org/content/11/9/1114.full.pdf+html>.

³ The NCCN cited to the European Journal of Cancer, *The device versus physician’s choice chemotherapy in recurrent glioblastoma: a randomised phase III trial of novel treatment modality* (2012; 48: 2192-2202). (See also Exh. 3).

⁴ NCCN, at https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx.

A Category 2B designation is “based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate,” indicating that at least 50 percent but less than 85 percent of the panel/voting participants supported the treatment option at the time.

LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

A party dissatisfied with a QIC's reconsideration may request an ALJ hearing. The party must file a written request for an ALJ hearing within sixty-five calendar days of the date on the QIC's reconsideration notice, and the requisite amount in controversy requirement must be met. 42 C.F.R. §§ 405.1000(a), 405.1002, and 405.1006.

B. Scope of Review

The issues before an ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in a party's favor. Here, the term "party" does not include a representative of CMS or one of its contractors that may be participating in the hearing. 42 C.F.R. § 405.1032(a).

C. Standard of Review

An ALJ conducts a de novo review and issues a decision based on the hearing record. 42 C.F.R. § 405.1000(d). Further, in addition to other binding authorities, an ALJ is governed by the Administrative Procedure Act (APA). 5 U.S.C. §§ 551 to 559 and 3105.

II. Principles of Law

A. Statutes & Regulations

The statutory authority for the Medicare program is found in Title XVIII of the Act. 42 U.S.C. § 1395 *et. seq.* The Medicare program is divided in multiple parts. Medicare Part B is a voluntary insurance program that provides medical insurance benefits to "aged and disabled individuals" for services not covered under Medicare Part A (or Part D). Act § 1831. The individual must elect to enroll in the program. *Id.* The program is financed through contributions appropriated by the Federal Government in addition to premium payments. *Id.* The Secretary of the Department of Health and Human Services has the authority to promulgate regulations which define or clarify the provisions of the Act. 42 C.F.R. § 410 *et seq.*

Section 1832 of the Act establishes the scope of benefits that are provided to an eligible beneficiary under Medicare Part B. *See also* 42 CFR §§ 410.3 and 410.10. Section 1832(a)(2)(B) of the Act indicates an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with a provider. Section 1861(s)(6) of the Act defines the term "medical and other health services" to include durable medical equipment. *See also* 42 CFR § 410.36(a)(3).

Medicare coverage for DME is determined in one of three ways. The claim must be decided consistent with an applicable "National Coverage Determination" (NCD). Act § 1869(c)(3)(B)(ii)(I). If there is no applicable NCD, the decision maker is required to consider, though is not bound, by the Local Coverage Determination ("LCD") for the

geographical area at issue. Act § 1869(c)(3)(B)(ii)(II). If there is no NCD or LCD addressing the matter, the decision maker is required to decide the matter “based on applicable information, including clinical experience and medical, technical, and scientific evidence.” Act § 1869(c)(3)(B)(ii)(III); *see also* 68 Fed. Reg. 63693.

The regulations define durable medical equipment as follows:

Equipment, furnished by a supplier or a home health agency that:

- 1) Can stand repeated use.
- 2) Effective with respect to items classified as DME after January 1, 2012, has an expected life of at least 3 years.
- 3) Is primarily and customarily used to serve a medical purpose.
- 4) Generally is not useful to an individual in the absence of an illness or injury.
- 5) Is appropriate for use in the home.

42 CFR § 414.202.

Section 1834 of the Act defines the rules for payment of durable medical equipment. *See also* 42 C.F.R. §§ 410.38(g) and 414.210.

Medicare may not make a payment under Part A or Part B for anything which is not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. Act § 1862(a)(1)(A); *see also* 42 C.F.R. §§ 411.15(k) and 414.200 *et seq.* A provider or supplier is responsible for providing sufficient documentation to support the services were medically necessary, the services were provided as bill, and that payment is due. Act §§ 1833(e); *see also* 42 C.F.R. § 424.5(a)(6).

In the event the services are found to be “not medically reasonable and necessary” or “custodial in nature” under Section 1862(a)(1) or (9) of the Act, Section 1879 of the Act provides for limitation on liability for Medicare payments. The regulations address how to determine if the beneficiary or provider/supplier had the requisite degree of knowledge to make them liable under Section 1879 of the Act. 42 C.F.R. § 411.400 *et seq.*; *see also HCFA Ruling 95-1.* If a beneficiary has no knowledge that the services would not be covered, but the provider/supplier of the services did, then the provider/supplier is liable and cannot seek or retain payment made by or on behalf of a beneficiary. 42 C.F.R. § 411.404. In general, the existence of a notice, manual, or community medical standard is sufficient to constitute finding the provider/supplier had notice. 42 C.F.R. § 411.406.

B. Policy and Guidance

Unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. Act § 1871(a)(2); *see also* 42 C.F.R. § 405.1060. An NCD is the Secretary’s determination on Medicare coverage for a particular item or services applied nationally. 42 C.F.R. § 405.1060(a). An ALJ is bound by the NCD and required to ensure the NCD is applied correctly when applicable. 42 C.F.R. § 405.1060(a), (b).

The Secretary has not issued an NCD specifically addressing the DME, or the related supplies, at issue in this case. CMS, *Medicare National Coverage Determinations (Internet-Only Manual Publ'n 100-03)*, ch. 1. See NCD § 280.1 *et seq.* regarding DME coverage in general.

CMS and its contractors are permitted to issue policy guidance describing criteria for coverage and payment of selected items and services. 42 C.F.R. § 405.1062. This guidance is located in Medicare's manuals and local coverage determinations ("LCD"). An ALJ is not bound by the policies outlined in a manual or LCD but is required to give the guidance substantial deference when applicable. 42 C.F.R. § 405.1062(a). An ALJ may decline to follow the guidance but must explicitly explain the reason(s) why. 42 C.F.R. § 405.1062(b). The ALJ's decision not to follow the policy applies only to the specific claim being considered and has no precedential effect on other claims. *Id.*

CMS and CGS Administrators had not published a LCD addressing the DME and related supplies as of the date(s) of service at issue.⁵

The *MPIM* indicates the Contractor is required to make individual claim determinations in the absence of an NCD and LCD. *MPIM (Internet-Only Manual Publ'n 100-08)*, ch. 13 § 13.3 (Jan. 2013). The decision is to be based on the medical reviewer's clinical judgement in light of the reasonable and necessary provisions outlined in Section 13.5.1. *Id.*

Reasonable and Necessary

Contractors shall describe in the draft LCD the circumstances under which the item or service is reasonable and necessary under 1862(a)(1)(A). Contractors shall consider a service to be reasonable and necessary if the contractor determines that the service is:

- Safe and effective;
- Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary); and
- Appropriate, including the duration and frequency that is considered appropriate for the item or service, in terms of whether it is:
 - o Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;
 - o Furnished in a setting appropriate to the patient's medical needs and condition;
 - o Ordered and furnished by qualified personnel;
 - o One that meets, but does not exceed, the patient's medical need; and
 - o At least as beneficial as an existing and available medically appropriate alternative.

There are several exceptions to the requirement that an item or service be reasonable and necessary for diagnosis or treatment of illness or injury. The exceptions appear in the full text of § 1862(a)(1).

MPIM, ch. 13 § 13.5.1; see also *Almy v. Sebelius*, 679 F.3d 297, 299 (4th Cir. 2012).

⁵ The Contractor did not draft an LCD addressing the The device and publish it for comments until after the date(s) of service.

The Contractor is required to use the “strong evidence available.” *MPIM*, ch. 13 § 13.7.1.

In order of preference, LCDs should be based on:

- Published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and
- General acceptance by the medical community (standard of practice), as supported by sound medical evidence based on:
 - o Scientific data or research studies published in peer-reviewed medical journals;
 - o Consensus of expert medical opinion (i.e., recognized authorities in the field); or
 - o Medical opinion derived from consultations with medical associations or other health care experts.

Acceptance by individual health care providers, or even a limited group of health care providers, normally does not indicate general acceptance by the medical community. Testimonials indicating such limited acceptance, and limited case studies distributed by sponsors with financial interest in the outcome, are not sufficient evidence of general acceptance by the medical community. The broad range of available evidence must be considered and its quality shall be evaluated before a conclusion is reached.

Id.

The *Medicare Benefits Policy Manual* (“*MBPM*”) defines reasonableness and necessity with regard to DME specifically. *MBPM (Internet-Only Manual Publ’n 100-2)*, ch. 15, § 110 (Oct. 2003). An item classified as DME will not be covered in every instance.”

MBPM, ch. 15, § 110.1.C. The item(s) must be “necessary and reasonable for treatment of an illness or injury, or to improve the functioning of a malformed body member.” *Id.* The *MBPM* states:

1 - Necessity for the Equipment

Equipment is necessary when it can be expected to make a meaningful contribution to the treatment of the patient's illness or injury or to the improvement of his or her malformed body member. In most cases the physician's prescription for the equipment and other medical information available to the DMERC will be sufficient to establish that the equipment serves this purpose.

2 - Reasonableness of the Equipment

Even though an item of DME may serve a useful medical purpose, the DMERC or intermediary must also consider to what extent, if any, it would be reasonable for the Medicare program to pay for the item prescribed. The following considerations should enter into the determination of reasonableness:

1. Would the expense of the item to the program be clearly disproportionate to the therapeutic benefits which could ordinarily be derived from use of the equipment?
2. Is the item substantially more costly than a medically appropriate and realistically feasible alternative pattern of care?
3. Does the item serve essentially the same purpose as equipment already available to the beneficiary?

3 - Payment Consistent With What is Necessary and Reasonable

Where a claim is filed for equipment containing features of an aesthetic nature or features of a medical nature which are not required by the patient's condition or where there exists a reasonably feasible and medically appropriate alternative pattern of care which is less costly than the equipment furnished, the amount payable is based on the rate for the equipment or alternative treatment which meets the patient's medical needs.

The acceptance of an assignment binds the supplier-assignee to accept the payment for the medically required equipment or service as the full charge and the supplier-assignee cannot charge the beneficiary the differential attributable to the equipment actually furnished.

Id.

The *MPIM* identifies what documentation a supplier is required to retain for at least a 7-year period. *MPIM*, ch. 5. The supplier is required to have an order from the physician prior to delivering the DME and/or related supplies. 42 C.F.R. § 410.38; *MPIM*, ch. 5, §§ 5.2.1, 5.2.2, and 5.2.3. The supplier must obtain a detailed written prior to filing a claim. *Id.* The supplier is required to maintain proof of delivery. *MPIM*, ch. 4, § 4.26.1 and ch. 5, § 5.8.

All Medical records must be authenticated by the author. *MPIM*, ch. 3, § 3.3.2.4. The method used shall be a handwritten or electronic signature, as stamped signatures are not acceptable. *Id.*

ANALYSIS

While this case primarily only deals with accessories for the TTFT device⁶, the overall issue is whether the TTFT device is medically reasonable and necessary in general for the treatment of recurrent GBM.⁷ Thus, this general determination turns on whether the TTFT device was merely investigational and experimental, or if it had been proven safe and effective, was widely accepted by the medical community, and appropriate for the treatment of RGBM. Thus, there are three main issues involved: (1) does the TTFT device meet the definition of DME; (2) does the TTFT device meet the requirements for medical necessity and efficacy generally; and (3) are the specific requirements to show medical necessity met in this case?

DME Determination

In general, for an item of DME to be covered by Medicare, it must be eligible for a defined Medicare benefit category, be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and meet all other applicable statutory and regulatory requirements. Act § 1862(a)(1)(A). The documentation must demonstrate the DME, and supplies, satisfy the medical reasonable and necessary standard. *MPIM*, ch. 5, § 5.7. The *MPIM* states the medical records should include information about a patient's diagnosis and other pertinent information to substantiate medical necessity for the type and quantity of items ordered as well as the frequency of use and replacement. *MPIM*, ch. 5, §§ 5.7 and 5.8.

⁶ The TTFT device is a piece of durable medical equipment and the insulated transducer arrays are required supplies for the system. The device is now known under the name, Optune® TTFT.

⁷ The term 'progressive' is used interchangeably with 'recurrent'.

It is uncontested that the TTFT device is DME that falls within a defined benefit category. CMS issued an interpretation or bulletin to this effect in July 2013.⁸ However, the mere status that the TTFT device was accepted as a piece of DME is not the primary inquiry in this case, and insufficient alone to achieve coverage.

General Requirements for Medical Necessity and Efficacy

In this case, there was no formal guidance in the form of an NCD or LCD addressing the DME (and supplies) at issue on the date(s) of service. Section 522 of the Benefits Improvement and Protection Act permits a contractor to issue a decision addressing whether and in what circumstances an item or service is covered as reasonable and necessary under Section 1862(a)(1)(A) of the Act. *MPIM*, ch. 13, §§ 13.1.3 and 13.5.1. The *MPIM* indicates the contractor “shall consider a services to be reasonable and necessary if the contractor determines that the services is:” (1) safe and effective; (2) not experimental or investigational; and (3) appropriate. *Id.* The contractor is to consider all applicable information when making a determination on a claim in those cases where there is no applicable NCD or LCD. Act § 1869(c)(3)(B)(i)(III).⁹

The appellant’s argument and testimony focused on the initial PMA showing that the TTFT device was proven at least as good as continued/repeat chemotherapy. The TTFT device resulted in a substantially better quality of life based on evidence that the device resulted in fewer adverse side effects. For example, the TTFT device usually only presented with a skin rash as a typical side effect, compared to the well-known systemic damage chemotherapy can cause.¹⁰

More central to this case, the appellant also presented findings associated with the EF-11 clinical trial, which was held prior to the dates of service. The EF-11 clinical trial initially comprised with 237 patients with RGBM. The overall survival rate of patients treated with TTFT was not superior but was comparable to the overall survival rate of patients treated with chemotherapy. Similarly, the FDA’s pre-market approval of TTFT for RGBM was based on the FDA’s conclusion, in its Summary of Safety and Effectiveness Data document, that “NovoTTF-100A treatment exhibits minimal toxicity, clinically comparable primary and secondary effectiveness and better quality of life compared to the chemotherapies in the control arm of the study.”¹¹

The FDA approved the appellant’s PMA in April 2011 for RGBM. It is noted that the panel of twelve physicians was split 6-6 on whether the device was effective,¹² but ultimately the chairperson’s vote resulted in the panels’ ultimate recommendation. The FDA presumably at least in part relied on the recommendation when it approved the PMA. To date, the FDA has not withdrawn the approval, or issued any warnings. While the NCCN did not immediately add TTFT treatment to its guidelines in 2011, the guidelines were changed to add TTFT as a treatment option in late 2012.

⁸ See NCD 280.1 generally.

⁹ NCD, ch. 1, § 280 et seq, governs DME in general. There are no provisions addressing TTFT.

¹⁰ Familiarity with the detailed, multi-hour general hearings are assumed, and cited *passim*. This is a mere paraphrase and not intended as a complete list of the parties/participant’s respective testimony. See Findings of Facts for more details. The hearing arguments and testimony also included substantial discussions about the nature of the PMA process, the PMA vote and subsequent events. These statements were considered and are discussed below.

¹¹ FDA PMA P100348, p. 38 (April 8, 2011).

¹² The panel voted unanimously that the device was safe. The panel ultimately recommended the NovoTTF-100A with a 7-3 vote (two members abstained from voting).

In summary, the record as a whole demonstrates by a preponderance of the evidence that the TTFT device was an appropriate treatment option for RGBM on the date(s) of service. The clinical studies and FDA approval establish that the TTFT device is, by a preponderance of the evidence, safe, not experimental or investigational, and appropriate in certain instances where a beneficiary is receiving treatment for RGBM.

Specific Requirements Needed to Demonstrate Medical Necessity

The appellant's burden is to prove by a preponderance of the evidence that the documentation submitted with the claim(s) satisfies six requirements. Failure to meet any of the six requirements means that appellant has failed to meet its burden. According to the FDA PMA approval:

This device is indicated for treatment of adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme, following histologically- or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GB after surgical and radiation options have been exhausted.

Additionally, the appellant's product dossier indicates the ideal treatment is for a patient to use the TTFT device 18 hours a day on average. This means a patient should use the TTFT device about 75 percent of the time prior to and/or during the dates of service. The medical record must specifically address a patient's compliance prior to and/or during the dates of service but some oral testimony may be used to explain or round out the data. However, oral testimony alone is insufficient because it does not comply with the *MPIM*. *MPIM*, ch. 5, §§ 5.7 and 5.8.

Thus, medical necessity would appear to contain six separate requirements. The six requirements are as follows:

- 1) the individual must be at least 22 years old;
- 2) the individual's medical history includes a diagnosis of GBM;
- 3) there is histological or radiological evidence of RGBM in the supratentorial region of the brain after the individual received chemotherapy;
- 4) the individual is not a candidate for further surgery or radiation; and
- 5) the TTFT is being used as a monotherapy.
- 6) the individual utilizes usage compliance of over 75%

The Instant Case

In the current case, the record confirms that appellant has satisfied the medical necessity requirements outlined above. Specifically in this case, there are two requirements that the beneficiary met: the requirement that the TTFT device is to be used as a monotherapy and that the individual meet usage compliance rates of over 75%. As mentioned above, on July 31, 2013, the beneficiary's physician signed a prescription for the TTFT device, lasting six months. During that timeframe, the beneficiary was seen by her physician and office visit notes clearly indicate that the beneficiary and physician were aware the TTFT device must be used as a

monotherapy. The beneficiary's physician noted that her last round of chemotherapy treatment was on July 2, 2013. The record does not indicate she was taking chemotherapy during any of the dates of service at issue.

Additionally, the usage compliance rates for the TTFT device are documented in the beneficiary's office visit notes. In September and October the medical record documents the beneficiary's usage compliance rates at 84% and 88%, respectively. The medical record must specifically address a patient's compliance prior to and/or during the dates of service; oral testimony alone is insufficient. Thus, there is documentation that the beneficiary was meeting the 75% compliance rate threshold on the dates of service at issue. As mentioned above, the appellant must meet all six requirements to meet the preponderance of the evidence burden. Because the appellant has submitted medical records that document the TTFT device requirements were satisfied, coverage by Medicare is appropriate.

Because the appellant is entitled to coverage for the TTFT device, the appellant is also entitled to coverage for the accessories and/or supplies related to the TTFT device. Thus, the associated supplies are also covered.

CONCLUSIONS OF LAW

Based upon a de novo review of the evidence and arguments presented, the following conclusions of law are made.

The record shows the DMEPOS at issue satisfied the applicable Medicare coverage criteria. The DMEPOS at issue are reasonable and necessary. It is therefore covered under Medicare Part B.

ORDER

The Medicare contractor is directed to process the claim in accordance with this decision.

SO ORDERED

Dated: **AUG 30 2018**


Andrew Henningfeld
Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City, Missouri

Appeal of:	OMHA Appeal No.: 1-8029669614
Enrollee:	Medicare: Part C
Medicare No.:	Before: Andrew Henningfeld Administrative Law Judge

DECISION

Based upon the evidence and arguments of record, a FULLY FAVORABLE decision is entered for the appellant.

PROCEDURAL HISTORY

Appellant is requesting coverage from a Medicare Advantage (MA) plan sponsor of an electrical stimulation device (Novocure/Optune) used for cancer treatment (HCPCS code E0766). Following an unfavorable initial determination, redetermination, and reconsideration, appellant timely filed a written request for an administrative law judge (ALJ) hearing. Appellant being a proper party and the amount in controversy being met, a hearing was held. The record is complete and this matter is ready for a decision.

ISSUES

Does coverage exist for the services at issue? If not, where does financial liability lie?

FINDINGS OF FACT

A detailed discussion of the facts in this case can be found in the hearing record and are incorporated herein.

(Ex. 2; Exh. 3; Exh. 4; Hearing testimony).

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

A party dissatisfied with an Independent Review Entity (IRE) reconsideration determination may request an ALJ hearing. The party must file a request for an ALJ hearing within sixty-five calendar days of the date on the IRE's reconsideration notice, and the requisite amount in controversy requirement must be met. 42 C.F.R. §§ 422.600, and 422.602.

B. Scope of Review

The issues before an ALJ include all the issues brought out in the coverage determination, redetermination, or reconsideration that were not decided entirely in an enrollee's favor. 42 C.F.R. § 405.1032(a).

C. Standard of Review

An ALJ conducts a de novo review and issues a decision based on the hearing record. 42 C.F.R. § 405.1000(d). Further, in addition to other binding authorities, an ALJ is governed by the Administrative Procedure Act (APA). 5 U.S.C. §§ 551 to 559 and 3105.

II. Principles of Law

A. Statutes, Regulations, and Guidance

A managed care organization offering an MA plan must provide enrollees with "basic benefits," which are all items and services covered by Medicare Part A and Part B available to beneficiaries residing in the plan's service area. 42 C.F.R. § 422.101(a). An MA plan "must provide enrollees in that plan with coverage of the basic benefits by furnishing the benefits directly or through arrangements, or by paying for the benefits." *Id.* at § 422.100(a). In providing "basic benefits," an MA organization must comply with national coverage determinations (NCDs) issued by the Centers for Medicare & Medicaid Services (CMS), "[g]eneral coverage guidelines included in original Medicare manuals and instructions unless superseded by operational policy letters or regulations in [part 422] or related instructions; and ... [w]ritten coverage decisions of local Medicare contractors." *Id.* at § 422.101(b).

ANALYSIS

All of the material in the record, including medical records and studies submitted by Appellant, have been reviewed as are incorporated in this decision. A comprehensive discussion of the facts and issues in this case can be found in the hearing. As such, the record confirms that coverage of the electrical stimulation device used for cancer treatment (HCPCS code E0766) during the dates of service at issue is appropriate in this case.

CONCLUSIONS OF LAW

Based upon a de novo review of the evidence and arguments presented, the following conclusions of law are made.

Coverage of the electrical stimulation device used for cancer treatment (HCPCS code E0766) at issue is appropriate.

ORDER

The Medicare plan sponsor is directed to process the claim in accordance with this decision.

SO ORDERED

Dated: **NOV 29 2018**


Andrew Henningfeld
Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, MO

Appeal of:

ALJ Appeal No.: 1-7903634831

Beneficiary:

Medicare: **Part B**

HICN:

Before: **Kim M. Hoffman**
U.S. Administrative Law Judge

I. SUMMARY OF DECISION

After carefully considering the evidence and arguments presented in the record, including the testimony presented at the hearing, a **FULLY FAVORABLE** decision is entered in favor of the appellant-beneficiary, (Appellant), with respect to claims for three months' rental of a device for administration of Tumor Treatment Field Therapy (TTFT). The electrical stimulation device (HCPCS code E0766) supplied to the beneficiary on September 8, 2017, October 8, 2017, and November 8, 2017, is covered and payable by Medicare Part B.

II. PROCEDURAL HISTORY

A. Prior Proceedings

The appellant submitted claims to CGS-DME MAC Jurisdiction C, the Medicare Administrative Contractor (Contractor) with jurisdiction, for coverage of three months' rental of an electrical stimulation device for cancer treatment (HCPCS code E0766-KFRR)¹ supplied to the beneficiary on September 8, October 8, and November 8, 2017. The Contractor denied the claim initially and upon redetermination based on its finding that tumor treatment field therapy (HCPCS code E0766) is categorically non-covered by Medicare because published medical studies failed to clearly document the effectiveness of the device.² The Contractor held the supplier responsible for the non-covered charges.

¹ The Centers for Medicare and Medicaid Services (CMS) developed the Healthcare Common Procedure Coding System (HCPCS) to establish "uniform national definitions of services, codes to represent services, and payment modifiers to the codes." 42 C.F.R. § 414.40(a). The HCPCS code E0766 denotes an "Electrical Stimulation Device Used for Cancer Treatment, Includes All Accessories, Any Type." See CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT)* (eff. Jan. 1, 2017) (LCD L34823). The "RR" modifier is added to indicate that the equipment was rented (rather than purchased). See CMS, *Medicare Claims Processing Manual (MCPM) (Internet-Only Manual Publ'n 100-4)* ch. 20, § 130.9. The "KF" modifier refers to an item designated by the U.S. Food and Drug Administration (FDA) as a class III device. See MCPM, ch. 20, § 30.9.

² The Contractor incorrectly cited LCD L33803 in support of its redetermination decision. (See Exh. 1, pp. 12-13.) That local coverage determination describes coverage criteria for urological supplies (urinary catheters, collection and drainage devices, and related supplies), not electrical stimulation devices for TTFT treatment. See CGS

On reconsideration, C2C Solutions, Inc., the Qualified Independent Contractor (QIC), affirmed the Contractor's decision as to both coverage and liability. Echoing the Contractor's reasoning, the QIC found that there was insufficient documentation to quantify the effects of the claimed device, currently published medical studies did not clearly document the device's effectiveness, and therefore the medical documentation did not support the need for the device.

Thereafter, the appellant timely requested an Administrative Law Judge (ALJ) hearing. The amount in controversy satisfies the jurisdictional requirement for an ALJ hearing pursuant to section 1869(b)(1)(E) of the Social Security Act (the Act).

B. Submission of Briefing and New Evidence

The beneficiary, through his authorized representative, submitted three additional pages of documentation and a CD containing various medical studies and administrative materials, under cover of a letter containing a statement of the beneficiary's position, with his request for ALJ hearing. (See Exh. 3, pp. 1-9.) The beneficiary's representative submitted a prehearing brief with supportive documentary attachments. (See Exh. 5, pp. 1-24.)

Though Medicare rules require a showing that good cause supports submission of new evidence for the first time at the OMHA level of review in appropriate circumstances, no such demonstration is required to permit admission of these materials. The prehearing brief and position paper constitute argument and advocacy rather than evidence. See generally 42 C.F.R. §§ 405.1018(c), 405.1028. Cf. *Elcommerce.com, Inc. v. SAP AG & SAP Am., Inc.*, No. 2011-1369, slip op. at 29 (Fed. Cir. Feb. 24, 2014) ("Attorney argument is not evidence."). Admission of the documentation and CD annexed to and/or accompanying these briefs, submitted by or on behalf of a beneficiary represented only by counsel (that is, by someone other than a provider or supplier) is appropriate under Medicare rules. See 42 C.F.R. § 405.1018(d).

The clinical studies, NCCN guidelines, FDA approvals, and other public-record documentation included on the CD comprise information that "can be accurately and readily determined from sources whose accuracy cannot reasonably be question" and as to which I can (and do) take judicial notice. See FED. R. EVID. 201(b). Moreover, admitting these materials serves the purpose of ensuring a complete record, the documentation is particularly relevant to the issues in this appeal, and the beneficiary's counsel asserts that medical records appended to the prehearing brief became "available [only] after the reconsideration request was submitted for this beneficiary." (Exh. 5, p. 1; compare 42 C.F.R. § 405.1028(a)(2)(v).) For all of the foregoing reasons, I have therefore determined to admit these materials to the administrative record, in Exhibits 3 and 5. (See Hearing CD.)

C. ALJ Hearing

A telephonic hearing was held on November 1, 2018. The beneficiary appointed Debra M. Parrish, Esq., to act as his representative in this appeal. Ms. Parrish participated on behalf of the beneficiary. Julie Miles, R.N., a clinical appeals specialist, and Dan McCoy, a case manager,

Administrators, LLC, *Urological Supplies* (eff. Jan. 1, 2017) (LCD L33803). The local coverage determination applicable to the device at issue is LCD L34823. This appears to have been a mere citation error.

appeared on behalf of Novocure Inc., the supplier of the device at issue. Ms. Parrish, Nurse Miles, and Mr. McCoy provided sworn testimony. Exhibits 1 through 5 were admitted without objection.

III. ISSUES

Whether all Medicare coverage requirements have been met, warranting payment under Title XVIII of the Social Security Act?

If the coverage requirements have not been met, whether the limitation on liability provisions of section 1879 of the Social Security Act are applicable?

IV. FINDINGS OF FACT

A. The Beneficiary and His Medical Record

On the first date of service, the male beneficiary was 67 years old. (See Exh. 1, p. 25; Exh. 2, pp. 5, 6, 8; Exh. 5, pp. 12, 14, 15-17.) In or about early March 2017, the beneficiary was found lying in his yard asleep with weakness and dizziness. (Exh. 1, p. 25; Exh. 2, p. 6; Exh. 5, pp. 12, 15.) He was taken to a local emergency room, where a CT scan performed on March 8, 2017, identified a large temporal lobe mass. (Exh. 1, p. 25; Exh. 2, pp. 5, 6; Exh. 5, p. 12.) The beneficiary was then transferred to Flowers Hospital, where he was admitted for inpatient care on March 8, 2017. (Exh. 2, p. 6; Exh. 5, pp. 12, 15-17.) An MRI of the brain performed the evening of his admission revealed an approximately 4.1 x 3.1 x 2.5 cm peripherally enhancing centrally hypointense mass in the right temporal lobe with surrounding vasogenic edema. (Exh. 1, p. 25; Exh. 2, pp. 5, 6, 7; Exh. 5, pp. 12, 13, 15.) A CT scan of the chest, abdomen, and pelvis the following day showed no evidence of metastatic disease. (Exh. 2, pp. 6, 7; Exh. 5, pp. 12, 13.) A second MRI of the brain the next day confirmed a 4 cm ring-enhancing lesion in the right temporal lobe. (Exh. 5, p. 17.)

The beneficiary underwent a craniotomy (a gross total resection) on March 11, 2017, with biopsy, the findings of which were consistent with, and following which he was newly diagnosed with, glioblastoma multiforme. (Exh. 1, p. 25; Exh. 2, pp. 5, 6; Exh. 5, pp. 12, 14, 21; Hearing CD.) The beneficiary subsequently underwent six weeks of concurrent chemotherapy (temozolomide) and radiation. (See Exh. 2, pp. 5, 8; Exh. 3, p. 1; Exh. 5, p. 14; Hearing CD.) That treatment was suspended three to four days during which the beneficiary required hospitalization for a seizure. (Exh. 2, p. 5.) The beneficiary subsequently completed that treatment on June 5, 2017. (Exh. 2, pp. 4, 5.)

In the meantime, an Optune™ Prescription Form set forth a “New Patient order” for the beneficiary to receive Optune (consisting of “(1) an Electric Field Generator (the ‘Device’); and (2) INE Insulated Transducer Arrays (the ‘Arrays’)” as well as “power supply items and accessories”) for six months to treat his glioblastoma (ICD-10 code C71.2). (Exh. 2, p. 1.) The form was signed by the beneficiary and his physician on May 30, 2017. (Exh. 2, pp. 1-2.) The beneficiary received training from a representative of the supplier on June 8, 2017, regarding the use of the Optune device. (Exh. 2, pp. 186-88.) The beneficiary took delivery of the equipment and began using TTFT therapy the same day. (See Exh. 1, p. 26; Exh. 2, pp. 184-85.)

The beneficiary presented to his physician, M.D., on July 25, 2017, for a follow-up visit. Progress notes reported that the beneficiary “has done well since treatment completion” and was doing well symptomatically, and that he remained on “maintenance temozolomide” as well as Optune therapy. They also noted that a July 13, 2017, MRI “identified overall stable findings.” (Exh. 2, p. 4.)

In an August 7, 2017, Medicare Appeals Request, Dr. explained that “Glioblastoma multiforme has the worst prognosis of any central nervous system (CNS) malignancy,” that its “[p]rognosis is poor, with a median survival time of approximately 14 months,” and that it “is very difficult to treat” due to the tumor cells’ resistance to conventional therapies, the risk of damage to the brain when using conventional therapy, the brain’s limited capacity to repair itself, and the inability of many drugs to cross the blood-brain barrier to act on the tumor. (Exh. 1, p. 26.) “Given the aggressive nature, and extremely limited treatment options of [this] disease, I recommended my patient receive coverage for Optune, as it is the best FDA approved option at this time for treating their glioblastoma.” (Exh. 1, pp. 25-26.) Dr. added that the beneficiary “had exhausted virtually all available treatments that could have been beneficial at the time of treatment” and that “[i]t is my professional opinion that Optune was the most promising treatment – if not only – option at the time.” (Exh. 1, p. 28.)

An MRI of the brain performed on June 5, 2018, revealed a slight decrease in size (compared to the previous examination) in the beneficiary’s right temporal lobe enhancing mass lesion (now measuring 25 mm x 9 mm x 11 mm) with a large area of stable T2 signal still present. (Exh. 5, pp. 18, 20.) The beneficiary had apparently experienced recent left-sided weakness. (Exh. 5, p. 18.) Progress notes from a follow-up visit with Dr. on July 23, 2018, reported that the beneficiary “seems to be overall doing well” and noted that “[h]e remains on Optune intermittently, but admittedly, he has decreased his overall compliance time with this.” (Exh. 5, p. 20.)

Progress notes from a September 18, 2018, follow-up examination with M.D., reported that the beneficiary, who was “now 18 months postop[,] . . . has an MRI scan which looks clear without evidence of progression of disease” and apparently showed “an area of enhancement in the right lateral temporal lobe which is unchanged.” (Exh. 5, pp. 21, 24.)

B. The Disease and the Device

Glioblastoma is a primary malignancy of the brain, a highly aggressive brain tumor frequently striking men and women at the peak of life, and the most prevalent primary malignant brain tumor in adults. (Exh 2, pp. 19, 72, 107.) At the end of 2015, the Journal of the American Medical Association (JAMA) reported that “[p]rognosis remains poor with no major treatment advance in more than a decade.” (Exh. 2, p. 19.) With optimal treatment, the median survival of individuals diagnosed with glioblastoma is 15 months from diagnosis. (Exh. 2, p. 107.) Standard treatment options include resection, chemotherapy, and radiation therapy. (Exh. 2, pp. 72-74.) Within nine months of initial treatment, most tumors recur. (Exh. 2, p. 107.) Treatment options after recurrence are generally limited and include repeat resection with possible implantation of carmustine wafers, additional radiation therapy, and chemotherapy. (Exh. 2, pp. 72-74, 107.)

Optune uses low-intensity electric fields to help slow or stop glioblastoma cancer cells from dividing. (Exh. 2, pp. 75, 107-8; Exh. 5, p. 2.) Four adhesive patches, or transducer arrays, are applied to the scalp and connected to the device and a battery to deliver the therapy. *See* Optune, *How Optune Works*, <https://www.optune.com/therapy/how-therapy-works>. According to the supplier's Product Dossier for Optune, the treatment is intended for adult patients who are 22 years of age or older with histologically-confirmed glioblastoma multiforme. (Exh. 2, pp. 61, 75; *see also* Exh. 2, p. 26.) For adult patients with newly-diagnosed, supra-tentorial glioblastoma, Optune coupled with temozolomide is indicated following maximal debulking surgery and completion of radiation therapy along with standard of care chemotherapy. (Exh. 2, p. 26.) Optune is indicated, according to the supplier's Product Dossier, for the treatment of recurrent glioblastoma following histologically or radiologically confirmed recurrence in the supra-tentorial region of the brain after receiving chemotherapy. (Exh. 2, pp. 61, 75; *see also* Exh. 2, p. 26.) For recurrent glioblastoma, Optune is intended to be used as a monotherapy and as an alternative to standard medical therapy for glioblastoma after surgical and radiation options have been exhausted. (*Id.*)

Optune, previously called NovoTTF-100A System, received FDA premarket approval for use in patients with recurrent glioblastoma on April 8, 2011. (Exh. 2, pp. 49-54, 61, 78; *see* FDA, Premarket Approval (PMA) database (Novo TTF-100A System), https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034A.pdf.) On October 5, 2015, the supplier received premarket approval from the FDA for use of Optune in patients newly diagnosed with glioblastoma. *See* FDA, Premarket Approval (PMA) database (Optune), https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034S013A.pdf. Ms. Parrish stated that TTFT, and specifically the Optune system, has been prescribed in all 50 states, the District of Columbia, and Puerto Rico, and obtained coverage by virtually every major payor in the United States. (Exh. 5, p. 4; *see also* Exh. 1, p. 27 (Dr. letter noting prevalence of insurers covering Optune); Exh. 3, p. 9 (July 23, 2018, Declaration of Justin Kelly, RN, BSN).)

C. Published Medical Studies

A number of published medical studies have been submitted to the administrative record. Among them, a 2012 article by two Harvard-affiliated neurologists described results of a phase III clinical trial of Optune's predecessor device for recurrent glioblastoma. (Exh. 2, pp. 117-21 (Ekokobe Fonkem & Eric T. Wong, NovoTTF-100A: A New Treatment Modality for Recurrent Glioblastoma, *Expert Rev. Neurother.* (2012)).) The neurologists reported that the clinical trials indicate that TTFT "has comparable efficacy, and less toxicity, when compared to conventional drug treatments in the recurrence setting." (Exh. 2, p. 120.) The results of this clinical trial supported FDA premarket approval for the use of the NovoTTF-100A device as monotherapy for recurrent glioblastoma. (*See* Exh. 2, pp. 117-18, 120.) In evaluating the clinical results, the authors found "a statistically significant survival advantage" offered by NovoTTF-100A "when compared to BSC chemotherapy" and opined that the device "may have a greater benefit to newly diagnosed patients than those with recurrent disease" given the genetic alterations in recurrent glioblastomas that render them more resistant to treatment. (Exh. 2, p. 120.)

Interim results of a later clinical trial for *newly diagnosed patients* showed significant improvement in outcomes of the patients, leading to crossover of trial subjects from the control

group to the experimental group. (Exh. 2, p. 17.) A November 2014 press release announcing an interim analysis of the study by The Society for NeuroOncology concluded that “[a]djuvant TMZ chemotherapy and NovoTTF provides a clinically and statistically significant improvement in progression-free and overall survival, and should become the new standard of care against” glioblastoma. (Exh. 2, p. 48.) On December 15, 2015, JAMA published an interim analysis of the results of this phase III clinical trial related to TTFT. (Exh. 2, pp. 13-22 (Roger Stupp, M.D. *et al.*, *Maintenance Therapy With Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma: A Randomized Clinical Trial*, 314 JAMA 2535-43 (Dec. 15, 2015)).) The analysis of the clinical trial concluded that adding TTFT to maintenance temozolomide chemotherapy in a population with new onset glioblastoma “significantly prolonged progression-free and overall survival.” (Exh. 2, pp. 14, 21.) After the study concluded, patients in the control group with ongoing maintenance therapy were offered TTFT therapy. (Exh. 2, p. 17.) Thirty-five of those patients chose to receive TTFT therapy. *Id.* A final analysis of the randomized phase III clinical trial in December 2017 concluded that “the addition of TTFields to maintenance temozolomide chemotherapy vs maintenance temozolomide alone, resulted in statistically significant improvement in progression-free survival and overall survival.” (Exh. 3, p. 9 (Optune Peer Reviewed Literature—Stupp JAMA 2017.pdf (Roger Stupp, M.D. *et al.*, *Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients With Glioblastoma: A Randomized Clinical Trial*, 318 JAMA 2306, 2306, 2315 (Dec. 19, 2017)); see Exh. 5, p. 3.)

The National Comprehensive Cancer Network (NCCN) included alternating electric field therapy for glioblastoma in its NCCN Clinical Practice Guidelines in Oncology for Central Nervous System Cancers (version 1.2016). (Exh. 2, pp. 9-12.) Use of alternating electric field therapy for recurrent glioblastoma was given a 2B rating (Exh. 2, p. 12), meaning that “[b]ased upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.” See NCCN, *NCCN Categories of Evidence and Consensus*, https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx [hereinafter *NCCN Categories*]. By the time of its 2018 updates to these guidelines, the NCCN had increased its rating for alternating electric field therapy (used in conjunction with standard RT and concurrent temozolomide and adjuvant temozolomide) to category 1 (see Exh. 3, p. 9 (NCCN_CNS_2018.pdf, at GLIO-3 to GLIO-4))—the NCCN’s highest rating, meaning that “[b]ased upon high-level evidence there is uniform NCCN consensus that the intervention is appropriate,” see *NCCN Categories*, *supra*.

V. LEGAL FRAMEWORK

A. ALJ Review Authority

1. Jurisdiction

Individuals or organizations dissatisfied with the reconsideration of an initial determination are entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act § 1869(b)(1)(A). See also 42 C.F.R. §§ 405.1002, 405.1006(b), 405.1014(c). The Secretary has delegated the authority to administer the

nationwide hearings and appeals system for the Medicare program to the Office of Medicare Hearings and Appeals. *See* 70 Fed. Reg. 36,386, 36,387 (June 23, 2005). The Administrative Law Judges within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

2. Scope of Review

The issues before the ALJ include all issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the appellant's favor. 42 C.F.R. § 405.1032(a). However, an ALJ may consider a new issue if its resolution could have a material impact on the claim or appealed matter and either (i) there is new and material evidence that was not available or known at the time of the earlier determination and that may result in a different conclusion or (ii) the evidence that was previously considered clearly shows on its face that an obvious error was made at the time of the earlier determination. 42 C.F.R. § 405.1032(b)(1). In that case, notice will be sent, before the start of the hearing, to those parties receiving the notice of hearing, and the parties will be given an opportunity to submit evidence regarding the issue. 42 C.F.R. § 405.1032(b).

3. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. 42 C.F.R. § 405.1000(d). A *de novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations, and to make an independent assessment based upon the evidence and controlling authorities. The burden of proving each element of a Medicare claim lies with the appellant and is by a preponderance of the evidence. *See* 5 U.S.C. § 556. Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, the conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a)(1). The decision must be based on evidence offered at the hearing or otherwise admitted into the record. *Id.*

B. Principles of Law

1. Statutes and Regulations

The statutory authority for the Medicare program is found in Title XVIII of the Social Security Act. 42 U.S.C. § 1395 *et seq.* The Supplementary Medical Insurance program (Part B of Title XVIII of the Act) provides coverage for various medical services and supplies furnished by physicians (or by others in connection with physicians' services), for outpatient hospital services, and for a number of other health-related items and services. *See* Social Security Act § 1832. *See also* 42 C.F.R. § 410.10. Section 1832(a)(1) of the Act provides for coverage under Medicare Part B to eligible beneficiaries for all or part of the cost of "medical and other health services," which section 1861(s)(6) defines to include "durable medical equipment[.]" *See also* 42 C.F.R. § 410.10(h). Claims for Medicare coverage of TTFT devices arise under Medicare's durable medical equipment (DME) benefit. *See* CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT) – Policy Article* (rev. eff. Jan. 1, 2017) (Policy Article A52711).

In accordance with section 1862(a)(1)(A) of the Act, Medicare may not make a payment under Part A or Part B for anything that is not reasonable and necessary for the diagnosis or treatment

of illness or injury or to improve the functioning of a malformed body member. *See also* 42 C.F.R. § 411.15(k)(1). Further, section 1833(e) of the Act makes clear that the provider or supplier is responsible for providing sufficient documentation to support that payment is due and the services were medically necessary and provided as billed. *See also* 42 C.F.R. § 424.5(a)(6). To be eligible for payment and to participate in the Medicare program, a supplier must provide Medicare with all information or documentation required to process its claim. *See* 42 C.F.R. §§ 424.57(b)(5), (c)(21).

Section 1879 limits the liability of the beneficiary and providers where payment may not be made because the items or services are not reasonable and necessary as required pursuant to section 1862(a)(1)(A) or are custodial in nature within the meaning of section 1862(a)(9), so long as neither the provider nor the beneficiary knew or could reasonably have been expected to know that payment would not be made for the claimed items or services. *See also* 42 C.F.R. §§ 411.400-.406; HFCA Ruling 95-1. Where the provider, but not the beneficiary, had such knowledge, beneficiary liability (but not provider liability) is limited through application of Medicare indemnification provisions. In general, the existence of a notice, manual, or community medical standard is sufficient to constitute notice to the provider. 42 C.F.R. § 411.406(e). Where the beneficiary knew or reasonably could have been expected to know of non-coverage, no payment is made, and the beneficiary will be found liable.

2. Policy and Guidance

Section 1871(a)(2) of the Social Security Act provides that no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of the benefits or payment for services under the Medicare program unless it is promulgated in the form of a validly adopted regulation. *See generally* 42 C.F.R. § 405.1060. NCDs are binding on ALJs, and an ALJ may not disregard or set aside an NCD. 42 C.F.R. §§ 405.1060(a)(4), (b). There is no NCD that controls the decision in this case.

Although not subject to the full force and effect of law,³ the Centers for Medicare and Medicaid Services (CMS) and CMS contractors have issued policy guidelines and local coverage determinations (LCDs) describing Medicare's coverage criteria for selected types of items and services. In this case, Local Coverage Determination L34823, issued by CGS Administrators, LLC, bears directly on the issue of Medicare Part B coverage for TTFT devices. LCD L34823 states unequivocally: "Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary." CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT)* (eff. Jan. 1, 2017) (LCD L34823).

On June 20, 2018, Novocure Inc., the supplier of the device at issue in this appeal, requested a formal reconsideration of LCD L34823. By letter dated August 7, 2018, a representative of the DME MAC Medical Directors advised that the current version of LCD L34823 "includes

³ Although not bound by a manual or LCD, the ALJ must give substantial deference to it if it is applicable to a particular case. When an ALJ declines to follow a manual or LCD, the ALJ decision must explain the reasons why the policy was not followed. 42 C.F.R. § 405.1062.

language indicating that the coverage of TTFT for recurrent glioblastoma multiforme (GBM) is not reasonable and necessary” but that “[c]overage of newly diagnosed GBM is not addressed.” (Exh. 3, p. 5; Exh. 5, p. 8.)

Medicare manuals provide guidance for determining whether a device is reasonable and necessary. The Medicare Program Integrity Manual (MPIM) suggests that a device is reasonable and necessary if it is:

- Safe and effective; and
- Not experimental or investigational; and
- Appropriate, including the duration and frequency that is considered appropriate for the item in terms of whether it is:
 - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient’s condition or to improve the function of a malformed body member;
 - Furnished in a setting appropriate to the patient’s medical needs and condition;
 - Ordered and furnished by qualified personnel;
 - One that meets, but does not exceed, the patient’s medical need; and
 - At least as beneficial as an existing and available medically appropriate alternative.

CMS, *Medicare Program Integrity Manual (MPIM) (Internet-Only Manual Publ’n 100-8)* ch. 13, § 13.5.1. Medicare instructs contractors as to the type of evidence to be used in making these technical determinations. Such decisions should be based on either “[p]ublished authoritative evidence” such as “definitive randomized clinical trials” and “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” *MPIM*, ch. 13, § 13.7.1. In all events, evaluations of reasonableness and necessity “shall be based on the strongest evidence available.” *Id.*

The Medicare Benefit Policy Manual (MBPM) provides guidance as to when durable medical equipment (DME) may be found to be reasonable and necessary. Equipment is necessary when it can be expected to make a meaningful contribution to the treatment of the patient’s illness or injury or to the improvement of his or her malformed body member. CMS, *Medicare Benefit Policy Manual (MBPM) (Internet-Only Manual Publ’n 100-2)* ch. 15, § 110.1(C)(1). As to reasonableness, even though an item of DME may serve a useful medical purpose, the Contractor must also consider to what extent it would be reasonable for the Medicare program to pay for the item prescribed, taking into consideration the following questions:

- Would the expense of the item to the program be clearly disproportionate to the therapeutic benefits which could ordinarily be derived from use of the equipment?
- Is the item substantially more costly than a medically appropriate and realistically feasible alternative pattern of care?
- Does the item serve essentially the same purpose as equipment already available to the beneficiary?

MBPM, ch. 15, § 110.1(C)(2).

Finally, the MPIM states that “LCDs which challenge the standard of practice in a community and specify that an item or service is *never* reasonable and necessary shall be based on sufficient evidence to *convincingly refute* evidence presented in support of coverage.” MPIM, ch. 13, § 13.7.1 (emphasis added). However, “[l]ess stringent evidence is needed when allowing for individual consideration.” *Id.*

VI. ANALYSIS

The beneficiary is challenging the denial of coverage for an electrical stimulation device for cancer treatment (HCPCS code E0766) that he rented in September, October, and November 2017. The governing local coverage determination, LCD L34823, states directly that the Contractor considers such devices to be categorically non-covered: “Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.” The Contractor and the QIC followed this guidance and denied coverage. (Exh. 1, pp. 4, 13.) Their reliance on the LCD’s plain and simple direction was understandable. However, after a thorough review of the administrative record, I find that the tumor treatment field therapy for treatment of the beneficiary’s glioblastoma on the dates of service at issue was medically reasonable and necessary within the meaning of section 1862(a)(1)(A) of the Social Security Act.

There is no National Coverage Determination specific to tumor treatment field therapy to guide the Contractor’s steps. While I would normally defer to an applicable LCD, I must decline to follow LCD L34823 in this case. First, the Contractor has already taken the position that “[c]overage of newly diagnosed GBM”—the condition for which the beneficiary seeks this therapy—“is not addressed” by the LCD. (Exh. 3, p. 5; Exh. 5, p. 8.) Moreover, as more fully set forth below, the record in this case clearly establishes that (1) the device qualifies as an item of durable medical equipment (which is a Medicare-covered benefit category), (2) the therapy has been shown to be safe and effective for use in patients (like the beneficiary) with newly diagnosed glioblastoma, (3) no alternative treatment modalities were available to the beneficiary, and (4) tumor treatment field therapy is medically reasonable and necessary to treat the beneficiary’s condition. Accordingly, the LCD’s categorical suggestion that the TTFT device can never be reasonable and necessary does not fit the facts of this case and must therefore be disregarded.

A. Medicare-Covered Benefit Category

Policy Article A52711 is as direct as LCD L34823. It categorically places the TTFT device in the durable medical equipment category of Medicare-covered benefits. According to the Policy Article, “[t]umor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act § 1861(s)(6)).” In fact, the Contractor provided the associated HCPCS code for the equipment and reported that the code (E0766) was in the frequent and substantial servicing payment category. *See* Policy Article A52711.

B. TTFT is Medically Reasonable and Necessary

The Medicare Program Integrity Manual instructs contractors to consider a service to be reasonable and necessary where that service is: (1) safe and effective; and (2) not experimental or investigational; and (3) appropriate (taking into account whether the service (a) is furnished in

accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member, (b) is furnished in a setting appropriate to the patient's medical needs and condition, (c) is ordered and furnished by qualified personnel, (d) meets, but does not exceed, the patient's medical need, and (e) is at least as beneficial as an existing and available medically appropriate alternative). *MPIM*, ch. 13, § 13.5.1.

1. *Safe and Effective Therapy*

Medicare does not pay for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury, or to improve the functioning of a malformed body member. Social Security Act § 1862(a)(1). To be reasonable and necessary, the procedure must be safe and effective and not experimental.

The Optune device received FDA premarket approval for use in patients with recurrent glioblastoma on April 8, 2011. (Exh. 2, pp. 50-54.) On October 5, 2015, the FDA gave premarket approval for use of Optune in patients (like the beneficiary) with newly diagnosed glioblastoma. FDA, Premarket Approval (PMA) database (Optune), https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034S013A.pdf. The FDA website explains that premarket approval ("PMA") entails the following:

PMA is the most stringent type of device marketing application required by FDA. The applicant must receive FDA approval of its PMA application prior to marketing the device. PMA approval is based on a determination by FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s).

FDA, *Premarket Approval (PMA)—Overview*, <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm>.

While FDA premarket approval does not establish that the device is medically reasonable and necessary pursuant to Medicare requirements, it does ensure that the FDA has closely examined the device and its application. In this case, the FDA determined that sufficient scientific evidence existed to provide the FDA with assurance that the device was safe and effective for its intended use in patients with both recurrent and newly diagnosed glioblastoma. This is wholly consistent with Medicare requirements. From this perspective, the use of the device meets Medicare guidance requiring that a device be proven safe and effective based on authoritative evidence. This also shows that the device is not experimental or investigational. The Contractor, however, looked to the FDA panel debate regarding the device to question its safety and effectiveness.

In June 2014, the Contractor published responses to comments it received regarding TTFT. In regard to the FDA approval of TTFT, the Contractor stated that while the FDA did approve the application with a positive vote of the FDA's Medical Device Advisory Committee's Neurological Devices Panel, the decision was split down the middle (six "yes" votes and six "no" votes) on the question of whether the device was effective for use. This vote was then

decided by a tie-breaking vote cast by the panel chairperson. See CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT) – Response to Comment Summary* (June 12, 2014), <https://www.cgsmedicare.com/jc/pubs/news/2014/0614/cope25909b.html>. While this is true, it does not negate the fact that the end result of the vote was that the FDA approved the use of the device as safe and effective.

The FDA's conclusion has only been fortified by medical investigation in the years that followed premarket approval. During that time, clinical studies evaluating the use and efficacy of the Optune device have resoundingly concluded that the device is safe and effective. Results from a phase III clinical trial utilizing TTFT in patients with newly diagnosed glioblastoma showed that the addition of TTFT to maintenance temozolomide chemotherapy "significantly prolonged progression-free and overall survival." (Exh. 2, pp. 14, 21.) With the benefit of two more years of assessment, a final analysis of the clinical trial results concluded that the addition of TTFT to maintenance chemotherapy "resulted in *statistically significant improvement* in progression-free survival and overall survival." (Exh. 3, p. 9 (emphasis added).) The results were so strong, even at first glance, that as early as November 2014, the Society for NeuroOncology was advocating that NovoTTF (Optune's predecessor) "should become the new standard of care against" glioblastoma. (Exh. 2, p. 48.) At the same time, the addition of TTFT to treat patients with newly diagnosed glioblastoma was not associated with any significant increase in systemic toxic effects or in the overall incidence, distribution, and severity of adverse events. (Exh. 2, p. 19.) Significantly, the study was promptly terminated as a result of its success—to allow all afflicted patients the opportunity to benefit from the apparent therapeutic benefits of TTFT—and patients in the control group in the JAMA-reported study did in fact cross over to the combined therapy group for TTFT treatment due to the improvement in outcomes seen. (Exh. 2, p. 17.) As Ms. Parrish noted, "the Data Safety Monitoring Board for the clinical trial for newly diagnosed glioblastoma found the data so compelling, they recommended early termination and allowing patients who were not receiving the treatment to be able to cross over and receive the treatment to be able to cross over and receive the treatment, and deeming it unethical to withhold it," and in a first, the "FDA agreed" to terminate "a brain tumor treatment trial . . . early based on positive results." (Exh. 5, p. 3.) These trials showed that the Optune device was safe and effective—and in particular for the treatment of the beneficiary's newly diagnosed glioblastoma.

2. *Not Experimental or Investigational*

The use of TTFT is generally accepted by the medical community. In the 2016 version of the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology for Central Nervous System Cancers, alternating electric field therapy is an option categorized as 2B for treatment of glioblastoma. (Exh. 2, p. 12.) Commenters presented the NCCN category 2B rating to the Contractor to suggest that TTFT should be covered as the standard of care, but the Contractor gave this little weight. In its June 2014 response to comments on TTFT, the Contractor suggested that the 2B rating (which signified "NCCN consensus"—but not "uniform NCCN consensus"—on the appropriateness of the intervention "[b]ased upon lower-level evidence") was not supported by "the highest level of evidence possible," the standard to which it felt bound in making coverage determinations. See CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT) – Response to Comment Summary* (June 12, 2014), <https://www.cgsmedicare.com/jc/pubs/news/2014/0614/cope25909b.html>. While CMS did not

address NCCN guidelines as they relate to medical devices for the treatment of cancer, the Contractor referenced the Medicare Benefit Policy Manual guidance regarding NCCN evidence for off-label use of drugs and biologicals. *See MBPM*, ch. 15, § 50.4.5. Under this MBPM guidance, the use of the drug would qualify as a medically accepted indication if the indication is a Category 1 or 2A in the NCCN, whereas a Category 3 indication in the NCCN would not qualify a use as medically accepted. *Id.*

I find that the MBPM guidance regarding off-label use of drugs and biologicals is misapplied when evaluating an FDA-approved medical device. If a drug is being used as approved by the FDA, it is not necessary to look to Medicare-approved compendia regarding off-label uses to further determine whether the use is appropriate. Off-label, as the name suggests, indicates that the specific use contemplated was not approved by the FDA. Here, the FDA approved the use of TTFT for recurrent glioblastoma as safe and effective. Further, the MBPM did not specifically address a category 2B classification by the NCCN. The NCCN category 2B definition suggests a 2B category showed lower-level consensus that the intervention is appropriate. “Generally-accepted” does not mean *uniformly* accepted, but instead something less stringent.

But in any event, the Contractor’s point now appears to be moot, because the NCCN has since upgraded its rating of alternating electric field therapy (in combination with chemotherapy and radiation) to category 1. (*See* Exh. 3, p. 9 (NCCN_CNS_2018.pdf, at GLIO-3 to GLIO-4).) As even the Contractor appeared to concede in 2014, this recognition of uniform consensus based on high-level evidence is the NCCN’s gold standard and supports coverage using “the highest level of evidence possible”. *Compare* CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT) – Response to Comment Summary* (June 12, 2014), <https://www.cgsmedicare.com/jc/pubs/news/2014/0614/cope25909b.html>. Moreover, this rating is embodied in treatment guidelines from a renowned national cancer organization (as opposed to evidence based on an individual physician treating a single patient in a clinical setting) and, as such, is particularly persuasive and authoritative. It provides convincing evidence that TTFT treatment is accepted in the medical community as safe and effective for the treatment of recurrent glioblastoma.

3. *TTFT is Appropriate for this Beneficiary*

Finally, it is necessary to evaluate the extent to which the electrical stimulation device was appropriate for the beneficiary and his care. *See MPIM*, ch. 13, § 13.5.1. Applying the considerations mandated by the MPIM, the record in this case convincingly demonstrates that it was.

Here, the item was furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient’s condition. The beneficiary had newly diagnosed glioblastoma multiforme. (Exh. 1, p. 25; Exh. 2, pp. 5, 6; Exh. 5, pp. 12, 14, 21; Hearing CD.) The FDA approved the use of the Optune device in adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy. FDA, Premarket Approval (PMA) database (Optune), https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034S013A.pdf. The beneficiary turned to

TTFT therapy with the Optune device after a gross total resection and a six-week course of concurrent chemotherapy and radiation, and (as suggested by the NCCN guidelines for maximum effectiveness) remained on maintenance temozolomide. (Exh. 2, pp. 4, 5, 6, 8; Hearing CD.) He “had exhausted virtually all available treatments that could have been beneficial at the time of treatment” and (in the judgment of his treating physician) “Optune was the most promising treatment – if not only – option at the time.” (Exh. 1, p. 28.)

Optune generally is a portable device used in the patient’s home (or other settings), which is appropriate for the beneficiary’s medical needs and condition. (Exh. 2, p. 29.) The device was ordered by the beneficiary’s treating physician and the device meets, but does not exceed, the beneficiary’s medical needs. (See Exh. 1, pp. 25-26, 28; Exh. 2, pp. 1-2.) Finally, the device is at least as effective as existing and available medically appropriate alternatives. This is evidenced by the beneficiary’s own clinical course. Notwithstanding clinical data reporting a median survival of 15 months (or less) from diagnosis among glioblastoma patients (Exh. 2, p. 107), results of a September 2018 MRI—18 months after the beneficiary’s craniotomy—“look[ed] clear without evidence of progression of disease.” (Exh. 5, p. 21.) Particularly considering that the beneficiary had exhausted all appropriate alternative conventional therapies, the Optune device would certainly meet the MPIM’s “appropriateness” standard for reasonableness and necessity. See *MPIM*, ch. 13, § 13.5.1.

One final aspect that must be considered is whether this device is substantially more costly than a medically appropriate and realistically feasible alternative pattern of care. In a notice of intent to publish a proposed rule and soliciting comments for criteria used to make local coverage decisions, the Health Care Financing Administration (HCFA) (CMS’s predecessor) stated that it was important for the Medicare program to be responsive to the rapid advances in health care. 65 Fed. Reg. 31,124, 31,125 (May 16, 2000). The HCFA notice advised that two criteria would likely be applied when making an NCD or LCD: the item or service must demonstrate (1) medical benefit and (2) added value to the Medicare population. *Id.* at 31,127. An item was defined to be medically beneficial if it produced “a health outcome better than the natural course of illness or disease with customary medical management of symptoms.” *Id.* In addition, “quality of life” was an acceptable health outcome named in the proposal. *Id.* One example of added value was “when a new item or service that falls within a Medicare benefit category would be medically beneficial for a beneficiary with a given clinical circumstance and there is no Medicare-covered medically beneficial alternative.” *Id.* This item or service “would add value to the program and we should cover it without consideration of costs during the coverage process.” *Id.* However, “[f]or clinically substitutable services, it is not reasonable or necessary to pay for incurred costs that exceed the cost of a Medicare-covered alternative that produces the same health outcome.” *Id.* at 31,128. Finally, if an equivalent service is “substantially more expensive than a Medicare-covered alternative,” cost considerations would lead to denial of coverage for the services. *Id.*

As reflected in the record, the beneficiary had exhausted the conventional, alternative treatment modalities for glioblastoma. (See Exh. 1, p. 28.) On March 11, 2017, the beneficiary underwent resection of the tumor. (Exh. 5, pp. 12, 14.) He followed surgery with a six-week course of temozolomide chemoradiation, which was complicated and interrupted by a seizure episode that sent him to the hospital. (Exh. 2, pp. 4, 5, 8; Exh. 3, p. 1; Exh. 5, p. 14; Hearing CD.) In early

June 2017, having exhausted alternative treatment modalities, the beneficiary started the use of the Optune device with maintenance chemotherapy (Exh. 1, p. 26; Exh. 2, pp. 4, 184-85) with impressive results (*see* Exh. 5, p. 21).

In short, when he began treatment with the Optune device, the beneficiary had already exhausted his other treatment options and had no feasible Medicare-covered alternative pattern of care available to halt the progression of his disease. After undertaking TTFT treatment, the beneficiary's disease progression stopped, which prolonged his lifespan well beyond the general prognosis and median survival prospects for a patient with newly diagnosed glioblastoma multiforme. The Optune device is admittedly expensive. (*See* Exh. 1, pp. 20-22.) The cost of this device, while high, does not outweigh both the evidence shown in clinical trials and the personal experience of the beneficiary with regard to suspending his disease progression.

For all of the foregoing reasons, I conclude that Optune (TTFT) has been shown to be safe and effective and is medically reasonable and necessary for the treatment of the beneficiary's condition.

VII. CONCLUSIONS OF LAW

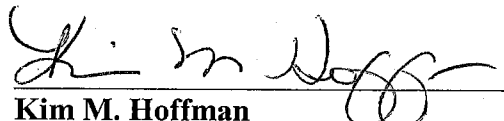
The decision in this case is **FULLY FAVORABLE**. I find that the electrical stimulation device for cancer treatment (HCPCS code E0766)—the Optune system—supplied to the beneficiary on September 8, October 8, and November 8, 2017, was medically reasonable and necessary for the treatment of the beneficiary's glioblastoma. The appellant's claims are covered by and payable under Medicare Part B.

VIII. ORDER

The Medicare contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: NOV 20 2018


Kim M. Hoffman
 U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, MO

Appeal of:

ALJ Appeal No.: **1-7865487873**

Beneficiary:

Medicare: **Part B**

HICN:

Before: **Kim M. Hoffman**
U.S. Administrative Law Judge

I. SUMMARY OF DECISION

After carefully considering the evidence and arguments presented in the record, including the testimony presented at the hearing, a **FULLY FAVORABLE** decision is entered in favor of the appellant-beneficiary, (Appellant), with respect to claims for four months' rental of a device for administration of Tumor Treatment Field Therapy (TTFT). The electrical stimulation device (HCPCS code E0766) supplied to the beneficiary on August 24, 2017, September 24, 2017, October 24 2017, and November 24, 2017, is covered and payable by Medicare Part B.

II. PROCEDURAL HISTORY

A. Prior Proceedings

The appellant submitted claims to CGS-DME MAC Jurisdiction C, the Medicare Administrative Contractor (Contractor) with jurisdiction, for coverage of four months' rental of an electrical stimulation device for cancer treatment (HCPCS code E0766) supplied to the beneficiary on August 24, 2017, September 24, 2017, October 24, 2017, and November 24, 2017. Making reference to Local Coverage Determination L34823 – Tumor Treatment Field Therapy, the Contractor denied the claim initially and upon redetermination based on its finding that tumor treatment field therapy (HCPCS code E0766) is non-covered by Medicare because published medical studies failed to clearly document the effectiveness of the device.

On reconsideration, C2C Solutions, Inc., the Qualified Independent Contractor (QIC), affirmed the Contractor's decision. The QIC similarly found that there was insufficient documentation to quantify the effects of the claimed device, currently published medical studies did not clearly document the device's effectiveness, and therefore the medical documentation did not support the need for the device.

Thereafter, the appellant timely requested an Administrative Law Judge (ALJ) hearing. The amount in controversy satisfies the jurisdictional requirement for an ALJ hearing pursuant to section 1869(b)(1)(E) of the Social Security Act (the Act).

B. Submission of Brief and New Evidence

Subsequent to filing her ALJ hearing request, the beneficiary, through her representative, submitted additional documentation including a pre-hearing brief, correspondence from the CMS Contractor, CGS, concerning the TTFT LCD L34823, and prior favorable decisions¹ on claims for TTFT therapy issued by OMHA².

To the extent the additional documentation is comprised of new evidence, I find good cause to admit this evidence into the record. 42 C.F.R. §§ 405.1018 and 405.1028. To the extent the additional documentation is comprised of argument, I admit this into the record. All of the additional documentation is admitted and is added to Exhibits 5 and 6.

C. ALJ Hearing

A telephonic hearing was held on October 11, 2018. Debra Parrish, Esq., the beneficiary's representative, participated on behalf of the beneficiary. Julie Miles, RN, a clinical appeals specialist, and Dan McCoy, a case manager, appeared on behalf of Novocure Inc.³, the supplier of the device at issue. Exhibits 1 through 6 were admitted without objection.

III. ISSUES

Whether all Medicare coverage requirements have been met, warranting payment under Title XVIII of the Social Security Act?

If the coverage requirements have not been met, whether the limitation on liability provisions of section 1879 of the Social Security Act are applicable?

IV. FINDINGS OF FACT

A. The Beneficiary and Her Medical Record

At the time of the dates of service, the female beneficiary was 69 years old. (Exh. 2, p. 4.) In January of 2017, the beneficiary presented to a community cancer center with an MRI showing a "3.2 cm ring enhancing intra-axial mass in the left frontal gyrus." On January 18, 2017, she underwent a maximal safe resection with final pathology confirming glioblastoma multiforme (GBM). A postoperative MRI confirmed a gross total resection. The beneficiary subsequently received adjuvant concurrent chemo-radiation March 7, 2017, through April 17, 2017. She tolerated her radiation therapy well and remained neurologically intact throughout her course. (Exh. 2, pp. 5-6.)

¹ It should be noted with regard to the prior favorable decisions that I am not, in any way, bound by these decisions.

² The pre-hearing brief and correspondence from the CMS Contractor, CGS, concerning the TTFT LCD L34823 were submitted in hard copy. The prior favorable decisions were submitted on CD. (Exhs. 5 and 6.)

³ Novocure is the manufacturer of the Optune system which is the TTFT device at issue.

On April 12, 2017, the beneficiary's oncologist, _____ wrote a prescription for Optune for a period of 6 months for a diagnosis of GBM (ICD-10 C71.1). Dr. _____ signed and dated the prescription on April 12, 2017. (Exh. 2, p. 14.) The desired treatment start date was noted to be May 10, 2017. (*Id.*)

On June 20, 2017, the beneficiary had an MRI of the brain. The MRI report was compared to prior MRI reports from January 17 and 19, 2017. (Exh. 2, p. 4.) It was noted that "[t]here is no suspicious nodular enhancement in or adjacent to the left frontal lobe resection cavity." (*Id.*) The testimony at the hearing was that, once use of the Optune system began, there was no progression of the beneficiary's tumor. And this was at a time when no other medical options were available for treatment of GBM. (Hearing CD.)

On September 26, 2017, Dr. _____ issued a renewal prescription for Optune for a period of 6 months for a diagnosis of GBM (ICD-10 C71.1). Dr. _____ signed and dated the prescription on September 26, 2017. (Exh. 2, p. 16.)

To date the beneficiary continues to use the Optune system and continues to remain clinically stable. (Hearing CD.)

B. The Disease and the Device

Glioblastoma is the most common form of primary brain cancer. Glioblastoma tumors are highly aggressive with survival, at initial presentation, of approximately 10 months - even with aggressive chemotherapy⁴. (Exh. 5, p. 2.) Medical literature, reports, and studies⁵ report that, for those diagnosed with GBM tumors, prognosis remains poor with no major treatment advance in more than a decade (as noted in 2015). With optimal treatment, the median survival is 15 months from diagnosis. Standard treatment options include resection, chemotherapy, and radiation therapy. Within nine months of initial treatment, most tumors recur. Treatment options after recurrence are generally limited and include repeat resection with possible implantation of carmustine wafers, additional radiation therapy, and chemotherapy. (Exh. 2, pp. 30-40, 66, 124-145, 160-187.)

Optune uses low-intensity electric fields to help slow or stop GBM cancer cells from dividing. Four adhesive patches, or transducer arrays, are applied to the scalp and connected to the device and a battery to deliver the therapy. See Optune, *How Optune Works*, <https://www.optune.com/therapy/how-therapy-works>. According to the supplier's Product Dossier for Optune, the treatment is intended for adult patients who are 22 years of age or older with histologically-confirmed GBM. For adult patients with newly-diagnosed, supra-tentorial glioblastoma, Optune coupled with temozolomide is indicated following maximal debulking surgery and completion of radiation therapy along with standard of care chemotherapy. Optune is indicated for the treatment of recurrent glioblastoma following histologically or radiologically confirmed recurrence in the supra-tentorial region of the brain after receiving chemotherapy. For recurrent glioblastoma, Optune is intended to be used as a monotherapy and as an alternative to

⁴ <https://rarediseases.info.nih.gov/diseases/2491/glioblastoma>

⁵ As found in the Journal of the American Medical Association (JAMA) and the Society for NeuroOncology, *inter alia*. (See generally Exh. 2, p. 26 *et seq.*)

standard medical therapy for glioblastoma after surgical and radiation options have been exhausted. (Exh. 2, pp. 41-65, 73-123.)

Optune, previously called NovoTTF-100A System, received FDA premarket approval for use in patients with recurrent glioblastoma on April 8, 2011⁶. On October 5, 2015, the supplier received premarket approval from the FDA for use of Optune in patients newly diagnosed with glioblastoma⁷. Ms. Parrish noted, at hearing, that TTFT, specifically the Optune system, is widely accepted and has been prescribed in all 50 states. (Hearing CD.) Furthermore, many private payors throughout the United States have approved coverage for treatment with the Optune system. (Exh. 2, p. 10.)

C. Published Medical Studies

A number of published medical studies are contained in the administrative record. Among them, a 2012 article by two Harvard-affiliated neurologists described results of a phase III clinical trial of Optune's predecessor device for recurrent glioblastoma⁸. (Exh. 2, pp. 135-139.) The neurologists reported that the clinical trials indicate that TTFT "has comparable efficacy, and less toxicity, when compared to conventional drug treatments in the recurrence setting." The results of this clinical trial supported FDA premarket approval for the use of the NovoTTF-100A device as monotherapy for recurrent glioblastoma. In evaluating the clinical results, the authors found "a statistically significant survival advantage" offered by NovoTTF-100A "when compared to BSC chemotherapy" and opined that the device "may have a greater benefit to newly diagnosed patients than those with recurrent disease" given the genetic alterations in recurrent glioblastomas that render them more resistant to treatment. (*Id.*)

Interim results of a later clinical trial for *newly diagnosed patients* showed significant improvement in outcomes of the patients, leading to crossover of trial subjects from the control group to the experimental group⁹. (Exh. 3, p. 8.) A November 2014, press release announcing an interim analysis of the study by The Society for NeuroOncology concluded that "[a]djuvant TMZ chemotherapy and NovoTTF provides a clinically and statistically significant improvement in progression-free and overall survival, and should become the new standard of care against" glioblastoma. (Exh. 2, p. 66.) On December 15, 2015, JAMA published an interim analysis of the results of this phase III clinical trial related to TTFT¹⁰. The analysis of the clinical trial concluded that adding TTFT to maintenance temozolomide chemotherapy in a population with new onset glioblastoma "significantly prolonged progression-free and overall survival." After the study concluded, patients in the control group with ongoing maintenance therapy were offered TTFT therapy. Thirty-five of those patients chose to receive TTFT therapy. (Exh. 2, pp.

⁶ FDA, Premarket Approval (PMA) database (Novo TTF-100A System), https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034A.pdf)

⁷ FDA, Premarket Approval (PMA) database (Novo TTF-100A System), https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034A.pdf)

⁸ Ekokobe Fonkem & Eric T. Wong, NovoTTF-100A: A New Treatment Modality for Recurrent Glioblastoma, *Expert Rev. Neurother.* (2012)

⁹ See "Article – Trail Halted Early.pdf". (Exh. 3, p. 8.)

¹⁰ Roger Stupp, M.D. *et al.*, *Maintenance Therapy With Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma: A Randomized Clinical Trial*, 314 JAMA 2535-43 (Dec. 15, 2015).

30-40.) A final analysis of the randomized phase III clinical trial in December 2017, concluded that “the addition of TTFields to maintenance temozolomide chemotherapy vs maintenance temozolomide alone, resulted in statistically significant improvement in progression-free survival and overall survival.”¹¹

The National Comprehensive Cancer Network (NCCN) included alternating electric field therapy for glioblastoma in its NCCN Clinical Practice Guidelines in Oncology for Central Nervous System Cancers (version 1.2016). Use of alternating electric field therapy for recurrent glioblastoma was given a 2B rating, meaning that “[b]ased upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.” By the time of its 2018 updates to these guidelines, the NCCN had increased its rating for alternating electric field therapy (used in conjunction with standard RT and concurrent temozolomide and adjuvant temozolomide) to category 1. (Exh. 2, pp. 26-29.)

V. LEGAL FRAMEWORK

A. ALJ Review Authority

1. Jurisdiction

Individuals or organizations dissatisfied with the reconsideration of an initial determination are entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act § 1869(b)(1)(A). *See also* 42 C.F.R. §§ 405.1002, 405.1006(b), 405.1014(c). The Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to the Office of Medicare Hearings and Appeals. *See* 70 Fed. Reg. 36,386, 36,387 (June 23, 2005). The Administrative Law Judges within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. (*Id.*)

2. Scope of Review

The issues before the ALJ include all issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the appellant’s favor. 42 C.F.R. § 405.1032(a). However, an ALJ may consider a new issue if its resolution could have a material impact on the claim or appealed matter and either (i) there is new and material evidence that was not available or known at the time of the earlier determination and that may result in a different conclusion or (ii) the evidence that was previously considered clearly shows on its face that an obvious error was made at the time of the earlier determination. 42 C.F.R. § 405.1032(b)(1). In that case, notice will be sent, before the start of the hearing, to those parties receiving the notice of hearing, and the parties will be given an opportunity to submit evidence regarding the issue. 42 C.F.R. § 405.1032(b).

¹¹ <https://www.ncbi.nlm.nih.gov/pubmed/29260225>

3. Standard of Review

The ALJ conducts a *de novo* review of each claim at issue. 42 C.F.R. § 405.1000(d). A *de novo* review requires the ALJ to review and evaluate the evidence without regard to the findings in the prior determinations, and to make an independent assessment based upon the evidence and controlling authorities. The burden of proving each element of a Medicare claim lies with the appellant and is by a preponderance of the evidence. See 5 U.S.C. § 556. Unless the ALJ dismisses the hearing, the ALJ will issue a written decision that gives the findings of fact, the conclusions of law, and the reasons for the decision. 42 C.F.R. § 405.1046(a)(1). The decision must be based on evidence offered at the hearing or otherwise admitted into in the record. *Id.*

B. Principles of Law

1. Statutes and Regulations

The statutory authority for the Medicare program is found in Title XVIII of the Social Security Act. 42 U.S.C. § 1395 *et seq.* The Supplementary Medical Insurance program (Part B of Title XVIII of the Act) provides coverage for various medical services and supplies furnished by physicians (or by others in connection with physicians' services), for outpatient hospital services, and for a number of other health-related items and services. See Social Security Act § 1832. See also 42 C.F.R. § 410.10. Section 1832(a)(1) of the Act provides for coverage under Medicare Part B to eligible beneficiaries for all or part of the cost of "medical and other health services," which section 1861(s)(6) defines to include "durable medical equipment[.]" See also 42 C.F.R. § 410.10(h). Claims for Medicare coverage of TTFT devices arise under Medicare's durable medical equipment (DME) benefit. See CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT) – Policy Article* (rev. eff. Jan. 1, 2017) (Policy Article A52711).

In accordance with section 1862(a)(1)(A) of the Act, Medicare may not make a payment under Part A or Part B for anything that is not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. See also 42 C.F.R. § 411.15(k)(1). Further, section 1833(e) of the Act makes clear that the provider or supplier is responsible for providing sufficient documentation to support that payment is due and the services were medically necessary and provided as billed. See also 42 C.F.R. § 424.5(a)(6). To be eligible for payment and to participate in the Medicare program, a supplier must provide Medicare with all information or documentation required to process its claim. See 42 C.F.R. §§ 424.57(b)(5), (c)(21).

Section 1879 limits the liability of the beneficiary and providers where payment may not be made because the items or services are not reasonable and necessary as required pursuant to section 1862(a)(1)(A) or are custodial in nature within the meaning of section 1862(a)(9), so long as neither the provider nor the beneficiary knew or could reasonably have been expected to know that payment would not be made for the claimed items or services. See also 42 C.F.R. §§ 411.400-.406; HFCA Ruling 95-1. Where the provider, but not the beneficiary, had such knowledge, beneficiary liability (but not provider liability) is limited through application of Medicare indemnification provisions. In general, the existence of a notice, manual, or community medical standard is sufficient to constitute notice to the provider. 42 C.F.R. §

411.406(e). Where the beneficiary knew or reasonably could have been expected to know of non-coverage, no payment is made, and the beneficiary will be found liable.

2. Policy and Guidance

Section 1871(a)(2) of the Social Security Act provides that no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of the benefits or payment for services under the Medicare program unless it is promulgated in the form of a validly adopted regulation. See generally 42 C.F.R. § 405.1060. NCDs are binding on ALJs, and an ALJ may not disregard or set aside an NCD. 42 C.F.R. §§ 405.1060(a)(4), (b). There is no NCD that controls the decision in this case.

Although not subject to the full force and effect of law,¹² the Centers for Medicare and Medicaid Services (CMS) and CMS contractors have issued policy guidelines and local coverage determinations (LCDs) describing Medicare's coverage criteria for selected types of items and services. In this case, Local Coverage Determination L34823, issued by CGS Administrators, LLC, bears directly on the issue of Medicare Part B coverage for TTFT devices. LCD L34823 states unequivocally: "Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary." CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT)* (eff. Jan. 1, 2017) (LCD L34823).

On June 20, 2018, Novocure Inc., the supplier of the device at issue in this appeal, requested a formal reconsideration of LCD L34823. By letter dated August 7, 2018, a representative of the DME MAC Medical Directors advised that the current version of LCD L34823 "includes language indicating that the coverage of TTFT for recurrent glioblastoma multiforme (GBM) is not reasonable and necessary" but that "[c]overage of newly diagnosed GBM is not addressed." (Exh. 3, p. 5; Exh. 5, p. 8.)

Medicare manuals provide guidance for determining whether a device is reasonable and necessary. The Medicare Program Integrity Manual (MPIM) suggests that a device is reasonable and necessary if it is:

- Safe and effective; and
- Not experimental or investigational; and
- Appropriate, including the duration and frequency that is considered appropriate for the item in terms of whether it is:
 - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;
 - Furnished in a setting appropriate to the patient's medical needs and condition;
 - Ordered and furnished by qualified personnel;
 - One that meets, but does not exceed, the patient's medical need; and

¹² Although not bound by a manual or LCD, the ALJ must give substantial deference to it if it is applicable to a particular case. When an ALJ declines to follow a manual or LCD, the ALJ decision must explain the reasons why the policy was not followed. 42 C.F.R. § 405.1062.

- At least as beneficial as an existing and available medically appropriate alternative.

CMS, *Medicare Program Integrity Manual (MPIM) (Internet-Only Manual Publ'n 100-8)*, ch. 13, § 13.5.1.

Medicare instructs contractors as to the type of evidence to be used in making these technical determinations. Such decisions should be based on either “[p]ublished authoritative evidence” such as “definitive randomized clinical trials” and “general acceptance by the medical community,” with the caveat that “[a]cceptance by individual health care providers” and “limited case studies distributed by sponsors with a financial interest in the outcome[] are not sufficient evidence of general acceptance by the medical community.” *MPIM*, ch. 13, § 13.7.1. In all events, evaluations of reasonableness and necessity “shall be based on the strongest evidence available.” *Id.*

The Medicare Benefit Policy Manual (MBPM) provides guidance as to when durable medical equipment (DME) may be found to be reasonable and necessary. Equipment is necessary when it can be expected to make a meaningful contribution to the treatment of the patient’s illness or injury or to the improvement of his or her malformed body member. CMS, *Medicare Benefit Policy Manual (MBPM) (Internet-Only Manual Publ'n 100-2)*, ch. 15, § 110.1(C)(1). As to reasonableness, even though an item of DME may serve a useful medical purpose, the Contractor must also consider to what extent it would be reasonable for the Medicare program to pay for the item prescribed, taking into consideration the following questions:

- Would the expense of the item to the program be clearly disproportionate to the therapeutic benefits which could ordinarily be derived from use of the equipment?
- Is the item substantially more costly than a medically appropriate and realistically feasible alternative pattern of care?
- Does the item serve essentially the same purpose as equipment already available to the beneficiary?

MBPM, ch. 15, § 110.1(C)(2).

Finally, the MPIM states that “LCDs which challenge the standard of practice in a community and specify that an item or service is *never* reasonable and necessary shall be based on sufficient evidence to *convincingly refute* evidence presented in support of coverage.” *MPIM*, ch. 13, § 13.7.1 (emphasis added). However, “[l]ess stringent evidence is needed when allowing for individual consideration.” *Id.*

VI. ANALYSIS

The beneficiary is challenging the denial of coverage for an electrical stimulation device for cancer treatment (HCPCS code E0766) that she rented in August, September, October, and November of 2017. The governing local coverage determination, LCD L34823, states that the Contractor considers such devices to be categorically non-covered: “Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.” As noted above, the

Contractor and the QIC followed this guidance and denied coverage. Their reliance on the LCD's plain and simple direction was understandable. However, after a thorough review of the administrative record, I find that the tumor treatment field therapy for treatment of the beneficiary's glioblastoma on the dates of service at issue was medically reasonable and necessary within the meaning of section 1862(a)(1)(A) of the Social Security Act.

There is no National Coverage Determination specific to tumor treatment field therapy to guide the Contractor's steps. While I would typically defer to an applicable LCD, I must decline to follow LCD L34823 in this case. First, the Contractor has already taken the position that "[c]overage of newly diagnosed GBM"—the condition for which the beneficiary seeks this therapy—"is not addressed" by the LCD. (Exh. 5, p. 4.) Moreover, as more fully set forth below, the record in this case clearly establishes that (1) the device qualifies as an item of durable medical equipment (which is a Medicare-covered benefit category), (2) the therapy has been shown to be safe and effective for use in patients (such as the beneficiary) with newly diagnosed glioblastoma, (3) no alternative treatment modalities were available to the beneficiary, and (4) tumor treatment field therapy is medically reasonable and necessary to treat the beneficiary's condition. Accordingly, the LCD's categorical suggestion that the TTFT device can never be reasonable and necessary does not fit the facts of this case and must therefore be disregarded.

A. Medicare-Covered Benefit Category

Policy Article A52711 is as direct as LCD L34823. It categorically places the TTFT device in the durable medical equipment category of Medicare-covered benefits. According to the Policy Article, "[t]umor treatment field therapy devices are covered under the Durable Medical Equipment benefit [Social Security Act § 1861(s)(6)]." In fact, the Contractor provided the associated HCPCS code for the equipment and reported that the code (E0766) was in the frequent and substantial servicing payment category. *See* Policy Article A52711.

B. TTFT is Medically Reasonable and Necessary

The Medicare Program Integrity Manual instructs contractors to consider a service to be reasonable and necessary when that service is: (1) safe and effective; and (2) not experimental or investigational; and (3) appropriate [taking into account whether the service (a) is furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member, (b) is furnished in a setting appropriate to the patient's medical needs and condition, (c) is ordered and furnished by qualified personnel, (d) meets, but does not exceed, the patient's medical need, and (e) is at least as beneficial as an existing and available medically appropriate alternative]. *MPIM*, ch. 13, § 13.5.1.

1. Safe and Effective Therapy

Medicare does not pay for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury, or to improve the functioning of a malformed body member. Social Security Act § 1862(a)(1). To be reasonable and necessary, the procedure must be safe and effective and not experimental.

The Optune device received FDA premarket approval for use in patients with recurrent glioblastoma on April 8, 2011. On October 5, 2015, the FDA gave premarket approval for use of Optune in patients (like the beneficiary) with newly diagnosed glioblastoma. The FDA website explains that premarket approval (“PMA”) entails the following:

PMA is the most stringent type of device marketing application required by FDA. The applicant must receive FDA approval of its PMA application prior to marketing the device. PMA approval is based on a determination by FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s).¹³

While FDA premarket approval does not establish that the device is medically reasonable and necessary pursuant to Medicare requirements, it does ensure that the FDA has closely examined the device and its application. In this case, the FDA determined that sufficient scientific evidence existed to provide the FDA with assurance that the device was safe and effective for its intended use in patients with both recurrent and newly diagnosed glioblastoma. This is wholly consistent with Medicare requirements. From this perspective, the use of the device meets Medicare guidance requiring that a device be proven safe and effective based on authoritative evidence. This also shows that the device is not experimental or investigational. The Contractor, however, looked to the FDA panel debate regarding the device to question its safety and effectiveness. In June 2014, the Contractor published responses to comments it received regarding TTFT. In regard to the FDA approval of TTFT, the Contractor stated that while the FDA did approve the application with a positive vote of the FDA’s Medical Device Advisory Committee’s Neurological Devices Panel, the decision was split down the middle (six “yes” votes and six “no” votes) on the question of whether the device was effective for use. This vote was then decided by a tie-breaking vote cast by the panel chairperson¹⁴. While this is true, it does not negate the fact that the end result of the vote was that the FDA approved the use of the device as safe and effective.

The FDA’s conclusion has only been buttressed by medical investigation in the years that followed premarket approval. During that time, clinical studies evaluating the use and efficacy of the Optune system have concluded that the device is safe and effective. Results from a phase III clinical trial utilizing TTFT in patients with newly diagnosed glioblastoma showed that the addition of TTFT to maintenance temozolomide chemotherapy “significantly prolonged progression-free and overall survival.” With the benefit of two more years of assessment, a final analysis of the clinical trial results concluded that the addition of TTFT to maintenance chemotherapy “resulted in *statistically significant improvement* in progression-free survival and overall survival.” The results were so strong that as early as November 2014, the Society for NeuroOncology was advocating that NovoTTF (Optune’s predecessor) should become the new standard of care against glioblastoma. At the same time, the addition of TTFT to treat patients with newly diagnosed glioblastoma was not associated with any significant increase in systemic toxic effects or in the overall incidence, distribution, and severity of adverse events.

¹³<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm>.

¹⁴ See CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT) – Response to Comment Summary* (June 12, 2014), <https://www.cgsmedicare.com/jc/pubs/news/2014/0614/cope25909b.html>.

Significantly, the study was promptly terminated as a result of its success—to allow all afflicted patients the opportunity to benefit from the therapeutic benefits of TTFT—and patients in the control group in the JAMA-reported study did in fact cross over to the combined therapy group for TTFT treatment due to the improvement in outcomes seen.

2. Not Experimental or Investigational

The use of TTFT is generally accepted by the medical community. In the 2016 version of the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology for Central Nervous System Cancers, alternating electric field therapy is an option categorized as 2B for treatment of glioblastoma. Commenters presented the NCCN category 2B rating to the Contractor to suggest that TTFT should be covered as the standard of care, but the Contractor gave this little weight. In its June 2014 response to comments on TTFT, the Contractor suggested that the 2B rating (which signified “NCCN consensus”—but not “uniform NCCN consensus”—on the appropriateness of the intervention “[b]ased upon lower-level evidence”) was not supported by “the highest level of evidence possible,” the standard to which it felt bound in making coverage determinations¹⁵. While CMS did not address NCCN guidelines as they relate to medical devices for the treatment of cancer, the Contractor referenced the Medicare Benefit Policy Manual guidance regarding NCCN evidence for off-label use of drugs and biologicals. See MBPM, ch. 15, § 50.4.5. Under this MBPM guidance, the use of the drug would qualify as a medically accepted indication if the indication is a Category 1 or 2A in the NCCN, whereas a Category 3 indication in the NCCN would not qualify a use as medically accepted. (*Id.*)

I find that the MBPM guidance regarding off-label use of drugs and biologicals is misapplied when evaluating an FDA-approved medical device. If a drug is being used as approved by the FDA, it is not necessary to look to Medicare-approved compendia regarding off-label uses to further determine whether the use is appropriate. Off-label, as the name suggests, indicates that the specific use contemplated was not approved by the FDA. Here, the FDA approved the use of TTFT for recurrent glioblastoma as safe and effective. Further, the MBPM did not specifically address a category 2B classification by the NCCN. The NCCN category 2B definition suggests a 2B category showed lower-level consensus that the intervention is appropriate. “Generally-accepted” does not mean *uniformly* accepted, but instead something less stringent.

But in any event, the Contractor’s point now appears to be moot, because the NCCN has since upgraded its rating of alternating electric field therapy (in combination with chemotherapy and radiation) to category 1. As even the Contractor appeared to concede in 2014, this recognition of uniform consensus based on high-level evidence is the NCCN’s gold standard and supports coverage using “the highest level of evidence possible”. Compare CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT) – Response to Comment Summary* (June 12, 2014), <https://www.cgsmedicare.com/jc/pubs/news/2014/0614/cope25909b.html>. Moreover, this rating is embodied in treatment guidelines from a renowned national cancer organization (as opposed to evidence based on an individual physician treating a single patient in a clinical setting) and, as such, is particularly persuasive and authoritative. It provides convincing evidence that TTFT

¹⁵ See CGS Administrators, LLC, *Tumor Treatment Field Therapy (TTFT) – Response to Comment Summary* (June 12, 2014), <https://www.cgsmedicare.com/jc/pubs/news/2014/0614/cope25909b.html>.

treatment is accepted in the medical community as safe and effective for the treatment of recurrent glioblastoma.

3. *TTFT is Appropriate for this Beneficiary*

Finally, it is necessary to evaluate the extent to which the Optune system was appropriate for the beneficiary and her care. *See MPIM*, ch. 13, § 13.5.1. Applying the considerations mandated by the MPIM, the record in this case convincingly demonstrates that it was.

Here, the item was furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition. The beneficiary had newly diagnosed GBM. The FDA approved the use of the Optune device in adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy. The beneficiary turned to TTFT therapy with the Optune device after a gross total resection and a course of chemo-radiation. As noted at hearing, when the beneficiary started TTFT therapy, she had no other available medical options for treatment of her GBM.

Optune generally is a portable device used in the patient's home (or other settings), which is appropriate for the beneficiary's medical needs and condition. The device was ordered by the beneficiary's treating physician. Finally, the device is at least as effective as existing and available medically appropriate alternatives. This is evidenced by the beneficiary's own clinical course. Notwithstanding clinical data reporting a median survival of 15 months (or less) from diagnosis among glioblastoma patients, to date, the beneficiary remains clinically stable. Particularly considering that the beneficiary had exhausted all appropriate alternative conventional therapies, the Optune system would certainly meet the MPIM's "appropriateness" standard for reasonableness and necessity. *See MPIM*, ch. 13, § 13.5.1.

One final aspect that must be considered is whether this device is substantially more costly than a medically appropriate and realistically feasible alternative pattern of care. In a notice of intent to publish a proposed rule and soliciting comments for criteria used to make local coverage decisions, the Health Care Financing Administration (HCFA) (CMS's predecessor) stated that it was important for the Medicare program to be responsive to the rapid advances in health care. 65 Fed. Reg. 31,124, 31,125 (May 16, 2000). The HCFA notice advised that two criteria would likely be applied when making an NCD or LCD: the item or service must demonstrate (1) medical benefit and (2) added value to the Medicare population. (*Id.* at 31,127.) An item was defined to be medically beneficial if it produced "a health outcome better than the natural course of illness or disease with customary medical management of symptoms." In addition, "quality of life" was an acceptable health outcome named in the proposal. One example of added value was "when a new item or service that falls within a Medicare benefit category would be medically beneficial for a beneficiary with a given clinical circumstance and there is no Medicare-covered medically beneficial alternative." This item or service "would add value to the program and we should cover it without consideration of costs during the coverage process." (*Id.*) However, "[f]or clinically substitutable services, it is not reasonable or necessary to pay for incurred costs that exceed the cost of a Medicare-covered alternative that produces the same health outcome." (*Id.* at 31,128.) Finally, if an equivalent service is "substantially more

expensive than a Medicare-covered alternative,” cost considerations would lead to denial of coverage for the services. (*Id.*)

As reflected in the record, the beneficiary had exhausted the conventional, alternative treatment modalities for her GBM. On January 18, 2017, the beneficiary underwent resection of the tumor. She followed surgery with a course of chemo-radiation. In May of 2017, the beneficiary started the use of the Optune system with impressive results.

In short, when she began treatment with the Optune system, the beneficiary had already had surgical resection of the tumor and a course of chemo-radiation and had no proven Medicare-covered alternative course of care available to halt the progression of the tumor. After undertaking TTFT treatment, the beneficiary’s disease progression stopped, which continues to prolong her lifespan well beyond the general prognosis and median survival prospects for a patient with newly diagnosed GBM. The Optune system is admittedly expensive. (Exh. 1, pp. 20-23.) The cost of this device, while high, does not outweigh both the evidence shown in clinical trials and the personal experience of the beneficiary with regard to suspending her disease progression.

For all of the foregoing reasons, I conclude that Optune (TTFT) has been shown to be safe and effective and is medically reasonable and necessary for the treatment of the beneficiary’s condition.

VII. CONCLUSIONS OF LAW

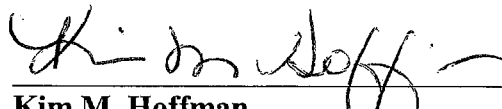
The decision in this case is **FULLY FAVORABLE**. I find that the electrical stimulation device for cancer treatment (HCPCS code E0766)—the Optune system—supplied to the beneficiary on August 24, 2017, September 24, 2017, October 24, 2017, and November 24, 2017, was medically reasonable and necessary for the treatment of the beneficiary’s glioblastoma. The appellant’s claims are covered by and payable under Medicare Part B.

VIII. ORDER

The Medicare contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: NOV 20 2018


Kim M. Hoffman
 U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Irvine Field Office
Irvine, CA

Appeal of: **NOVACURE**

ALJ Appeal No.: **1-2813459974**

Beneficiary:

Medicare: **Part C**

HICN: *******4586A**

Before: **E. M. Koldewey**
U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented in the administrative record and at the hearing, a **FULLY FAVORABLE** decision is entered in the matter of **Novacure (Appellant)** on behalf of Medicare Beneficiary **REDACTED** (Beneficiary/Enrollee).

PROCEDURAL HISTORY

The Medicare Beneficiary was enrolled in Humana Health Plan., a Medicare Advantage health plan ("Plan"), at the time of services at issue. (Exh. 1). He requested that his Plan pre-approve a tumor treatment field therapy (TTFT) device. On September 29, 2014, the Plan issued a denial for the approval on the grounds that per LCD L34665¹, TTFT (E0766) is denied as not reasonable and necessary. (Exh. 3, p. 42). Appellant appealed. On October 10, 2014, the Plan affirmed its denial and forwarded the appeal to an Independent Review Contractor, Maximus Federal Services Managed Care & PACE Reconsideration Project, for further review. (Exh. 3, p. 34). On October 14, 2014, Maximus² affirmed the Plan's unfavorable determination, finding that the Plan did not have pre-approve the tumor treatment field therapy (TTFT) device. (Exh. 3, p. 14).

The Appellant's request for a hearing before an Administrative Law Judge (ALJ) was received by the Office of Medicare Hearings and Appeals (OMHA) on December 5, 2014. (Exh. 3, p. 9). The appeal was timely filed and the amount in controversy met the jurisdictional requirements. *See* 42 C.F.R. § 405.1006; *see also* 75 Fed. Reg. 59138 (Sep. 23, 2011).

¹ In its September 2014 denial, the Plan referred to the TTFT LCD as LCD L34665 but in its October 2014 denial, the Plan referred to LCD 34730. Both LCDs refer to E0766 which is the service at issue.

² Maximus refers to the LCD for E0766 as LCD L34823; however, this LCD was not effective for the date of service at issue. For the purpose of this decision, the LCD that is being referenced is LCD L34730 which is applicable for Connecticut.

Pursuant to written notice, a telephonic administrative hearing was held on the Appellant's claim at OMHA in Irvine, California, on February 12, 2015. Hearing CD. REDACTED case manager, and REDACTED associate director, represented the Appellant. The Plan was represented by K. Jewell and Dr. C. McGuire-Dunn. Good cause was found for admission of Dr. REDACTED letter pursuant to 42 C.F.R. §§405.1018 & 405. All numbered exhibits (marked as Exhibits 1 through 10) were admitted into the evidentiary record without objection.

ISSUES

The hearing concerns the general issue of whether all Medicare coverage requirements are met for the services and/or supplies at issue, i.e., whether payment can be made under Title XVIII of the Social Security Act. The more specific issue is:

1. Is there sufficient evidence in the administrative record to establish that Humana Health Plan Inc. is required to pre-approve a tumor treatment field therapy (TTFT) device for REDACTED REDACTED pursuant to Medicare Part C and the Plan's Evidence of Coverage? REDACTED

FINDINGS OF FACT

The following facts are established by a preponderance of the evidence:

The Medicare enrollee, a 44 year old male, was diagnosed with recurrent atypical grade II meningioma. In 1983, at age 13, he underwent a resection with shunt placement and radiation to treat three ependymomas. In 2002, he was diagnosed with right parasagittal meningioma WHO grade I and underwent a resection and gamma knife. He suffered a recurrence in 2008. In 2012, enrollee underwent a craniotomy and resection. In August 2013, he suffered from seizures and was noted to have several dural based masses consistent with recurrent meningioma and was started on Ilydrea. In January 2014, he began DIME infusional chemotherapy and CIVI-CAD chemotherapy. In September 2014, enrollee's physician, REDACTED MD, prescribed Novo TTF. Dr. REDACTED determined that it was the best FDA approved option at this time for treating recurrent atypical grade II meningioma.

There is a letter of medical necessity submitted by Dr. REDACTED dated September 17, 2014, requesting expedited review request for authorization of benefits coverage for a tumor treatment field therapy (TTFT). (Exh. 3, pp. 45-47).

In September 2014, Enrollee requested that his health plan, Humana, pre-approve a tumor treatment field therapy (TTFT) device. On September 29, 2014, the Plan issued a denial for the approval on the grounds that per LCD L34655 TTFT (E0766) is denied as not reasonable and necessary. (Exh. 3, p. 42). Appellant appealed. The Plan affirmed its denial and forwarded the appeal to an Independent Review Contractor, Maximus Federal Services Managed Care & PACE Reconsideration Project, for further review. (Exh. 3, p. 14). On October 14, 2014, Maximus affirmed the Plan's unfavorable determination, finding that the Plan did not have pre-approve a tumor treatment field therapy (TTFT) device finding that LCD 34823 states that tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. *Id.*

LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (“HHS”), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Sections 1852(g) and 1869(b)(1)(A) of the Act.

In implementing this statutory directive, the Secretary has delegated her authority to administer the nationwide hearings and appeals systems for the Medicare program to OMHA. *See* 70 Federal Register 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *Id.*

A hearing before an ALJ is available only if the remaining amount in controversy is \$140 or more. 42 C.F.R. § 405.1006; *see also* 75 Fed. Reg. 59138 (Sep. 23, 2011). The request for hearing is timely filed if filed within 60 calendar days after receipt of the QIC’s decision. 42 C.F.R. § 405.1002.

B. Scope of Review

Under the Centers for Medicare and Medicaid Services’ (“CMS”) implementation policy for the Medicare, Medicaid, SCHIP Benefits Improvement and Protection Act of 2000 (“BIPA”), Pub. Law 106-554, app. F, 114 Stat. 2763, 2763A-463, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (“MMA”), Pub. Law 108-173, 117 Stat. 2066, when considering Medicare appeals, all initial determinations by CMS contractors, subsequent to January 1, 2006 and all appeals that were subject to a QIC reconsideration, are governed by the ALJ hearing procedures set forth at 42 C.F.R. §§ 405.1000 through 405.1064. *See* 70 Fed. Reg. 11420, 11424-26 (Mar. 8, 2005).

The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in the Appellant's favor. However, if evidence presented before or during the hearing causes the ALJ to question a favorable portion of the determination, he or she may notify the parties before the hearing and may consider it an issue at the hearing. 42 C.F.R. § 405.1032(a).

C. Standard of Review

An ALJ conducts a *de novo* review and issues a decision based on the hearing record. 42 C.F.R. § 405.1000(d). A *de novo* review means the ALJ reviews the evidence without regard to the findings in the prior determinations on the claim and makes an independent assessment based on the evidence and the controlling laws. However, the burden of proving each element of a Medicare claim lies with the Appellant and is satisfied by submitting sufficient evidence in accordance with Medicare rules. *See e.g.*, Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; *see also* 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, .1030.

An Appellant may offer new evidence for the first time at the ALJ level of appeal only upon a showing of good cause why the evidence was not submitted to the QIC or a prior decision maker. 42 C.F.R. § 405.1018. The ALJ will determine whether good cause exists for the late submission of the new evidence and may only consider the evidence in making a decision if good cause is found. *See also* 42 C.F.R. §§ 405.1028 and 405.1030. This late evidence restriction does not apply to unrepresented beneficiaries.

If the evidence in the hearing record supports a finding in favor of appellant(s) on every issue, the ALJ may issue a hearing decision without giving the parties prior notice and without holding a hearing. The notice of the decision informs the parties that they have the right to a hearing and a right to examine the evidence on which the decision is based. *See* 42 C.F.R. § 405.1038. The decision of the ALJ is generally binding on all parties to the hearing. *See* 42 C.F.R. § 405.1048.

II. Principles of Law

A. Statutes and Regulations

Title XVIII of the Act, as amended (42 U.S.C. §1395 *et seq.*), establishes a federally subsidized health insurance program (“Medicare”) to be administered by the Department of Health and Human Services. Eligibility for Medicare benefits is determined under Title XVIII of the Act and the federal regulations set forth in Title 42 of the Code of Federal Regulations (“C.F.R.”).

The Medicare Part C program establishes standards and sets forth the requirements, limitations, and procedures for Medicare services furnished, or paid for, by Medicare Advantage (“MA”) organizations through MA plans. *See* Act § 1851 *et seq.*; *see also* 42 C.F.R. § 422.1 *et seq.* A person is eligible to enroll in Part C if s/he is entitled to Medicare Part A and enrolled in Part B, has not been medically determined to have end-stage renal disease, and meets the applicable residency requirements. Act § 1851; 42 C.F.R. § 422.50(a).

An MA organization (“MAO”) offering an MA plan must provide enrollees in that plan with coverage for basic benefits (all Medicare covered services) by furnishing the benefits directly, through arrangements or by paying for such benefits, and CMS reviews the benefits. 42 C.F.R. §§ 422.100(a) and 422.101(a).

MAOs that offer coordinated care plans, such as the MA plan, may specify the network of providers from whom enrollees may obtain services, if the organization ensures that all covered services are available and accessible under the plan. Act § 1852(d); 42 C.F.R. § 422.112(a). To accomplish this, the MAO must maintain and monitor a network of appropriate providers that is supported by written agreements and is sufficient to provide adequate access to covered services to meet the needs of the population served as well as provide or arrange for necessary specialty care. 42 C.F.R. § 422.112(a). An MAO must also arrange for specialty care outside of the plan provider network when network providers are unavailable or inadequate to meet an enrollee’s medical needs. *Id.* MA plan networks are approved by CMS to ensure that all applicable requirements are met, including access, availability, service areas and quality. 42 C.F.R. § 422.4.

B. Policy and Guidance

Section 1871(a)(2) of the Act provides that no rule, requirement or statement of policy, other than a national coverage determination (“NCD”), can establish or change a substantive legal standard governing the scope of the benefits or payment for services under the Medicare program unless promulgated as a regulation by CMS. *See also* 42 C.F.R. § 405.860. NCDs promulgated by the Secretary of HHS under the authority of § 1862(a)(1) of the Act dictate the criteria under which Medicare covers specified services, procedures or supplies. NCDs are binding upon ALJs. 42 C.F.R. § 405.732(a)(4). “An ALJ may not disregard, set aside or otherwise review an NCD.” 42 C.F.R. § 405.732(b)(1).

Although not subject to the force and effect of law, CMS and its contractors have issued policy guidelines, including manuals and local coverage determinations (“LCDs”), which describe coverage guidelines for selected types of medical items and services. The respective manuals issued by CMS provide guidance in the administration of the Medicare program. In *Shalala v. Guernsey Memorial Hospital*, 514 U.S. 87, 102 (1995), the United States Supreme court concluded that an agency manual section is a valid interpretive rule and that it is reasonable for the agency to follow it.

In providing “basic benefits,” an MAO must comply with NCDs, “[g]eneral coverage guidelines included in original Medicare manuals and instructions unless superseded by operational policy letters or regulations . . . ,” and LCDs issued by Medicare contractors with jurisdiction for claims in the geographic area.³ 42 C.F.R. § 422.101(b).

Pursuant to 42 C.F.R. § 405.1062(a), an ALJ is not bound by a manual or LCD, but will give substantial deference to it if it is applicable to a particular case. According to 42 C.F.R. § 405.1062(b), if an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. An ALJ decision to disregard such a policy applies only to the specific claim being considered and does not have precedential effect.

The Medicare Policy Integrity Manual Chapter 13 states the following:

13.5.1 - Reasonable and Necessary Provisions in LCDs

(Rev. 473, Issued: 06-21-13, Effective: 01-15-13, Implementation: 01-15-13)

An item or service may be covered by a contractor LCD if:

- It is reasonable and necessary under 1862(a)(1)(A) of The Act. Only reasonable and necessary provisions are considered part of the LCD.

Reasonable and Necessary

Contractors shall describe in the draft LCD the circumstances under which the item or service is reasonable and necessary under 1862(a)(1)(A). Contractors shall consider a service to be reasonable and necessary if the contractor determines that the service is:

- Safe and effective;
- Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary); and

³ MA plans covering more than one local coverage geographic area may adopt the local policy that is most beneficial to MA enrollees as a uniform policy for all plan enrollees. 42 C.F.R. § 422.101(b)(3).

- Appropriate, including the duration and frequency that is considered appropriate for the item or service, in terms of whether it is:
 - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;
 - Furnished in a setting appropriate to the patient's medical needs and condition;
 - Ordered and furnished by qualified personnel;
 - One that meets, but does not exceed, the patient's medical need; and
 - At least as beneficial as an existing and available medically appropriate alternative.

There are several exceptions to the requirement that an item or service be reasonable and necessary for diagnosis or treatment of illness or injury. The exceptions appear in the full text of §1862(a)(1) and include but are not limited to:

- Pneumococcal, influenza and hepatitis B vaccines are covered if they are reasonable and necessary for the prevention of illness;
- Hospice care is covered if it is reasonable and necessary for the palliation or management of terminal illness;
- Screening mammography is covered if it is within frequency limits and meets quality standards;
- Screening pap smears and screening pelvic exam are covered if they are within frequency limits;
- Prostate cancer screening tests are covered if within frequency limits;
- Colorectal cancer screening tests are covered if within frequency limits; and
- One pair of conventional eyeglasses or contact lenses furnished subsequent to each cataract surgery with insertion of an interlobular lens;

LCD L34730, Tumor Treatment Field Therapy (TTFT) states the following relevant sections:

Coverage Indications, Limitations, and/or Medical Necessity

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements. For the items addressed in this local coverage determination, the criteria for "reasonable and necessary", based on Social Security Act § 1862(a)(1)(A) provisions, are defined by the following coverage indications, limitations and/or medical necessity.

For an item to be covered by Medicare, a detailed written order (DWO) must be received by the supplier before a claim is submitted. If the supplier bills for an item addressed in this policy without first receiving the completed DWO, the item will be denied as not reasonable and necessary.

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

C. Evidence of Coverage

The Plan's EOC explains that the Plan covers items and services in accordance with Medicare rules. Exh. 1

ANALYSIS

The primary issue on appeal is whether Humana Health Plan Inc. is required to pre-approve a tumor treatment field therapy (TTFT) device for [REDACTED] pursuant to Medicare Part C and the Plan's Evidence of Coverage. Based on a review of the evidence, the undersigned ALJ finds that the Plan is required to pre-approve a tumor treatment field therapy (TTFT) device for [REDACTED] pursuant to Medicare Part C and the Plan's Evidence of Coverage.

Maximus determined that the Plan was not required to pre-approve the TTFT device finding that the requested service is not medically necessary under Medicare and the Humana plan and upheld the determination. Maximus determined that according to LCD L34730, TTFT (E0766) will be denied as not reasonable and necessary.

Pursuant to Medicare rules, a Medicare Advantage plan must provide its enrollees with coverage for all services covered by regular Medicare. *See* 42 CFR §422.101. The Plan's Evidence of Coverage also states that the Plan covers items and services in accordance with Medicare rules. In addition, LCD L34730, states that tumor treatment field therapy (TTFT)(E0766) will be denied as not reasonable and necessary.

In this case, the Medicare Enrollee, a [REDACTED], was diagnosed with recurrent atypical grade II meningioma. In 1983, at age 13, he underwent a resection with shunt placement and radiation to treat three ependymomas. In 2002, he was diagnosed with right parasagittal meningioma WHO grade I and underwent a resection and gamma knife. He suffered a recurrence in 2008. In 2012, Enrollee underwent a craniotomy and resection. In August 2013, he suffered from seizures and was noted to have several dural based masses consistent with recurrent meningioma and was started on Hydrea. In January 2014, he began DIME infusional chemotherapy and CIVI-CAD chemotherapy. Then in September 2014, Enrollee's physician, [REDACTED] MD, prescribed Novo TTFT. Dr. [REDACTED] determined that it was the best FDA approved option at this time for treating recurrent atypical grade II meningioma.

At the hearing, Appellant's representatives corroborated Dr. [REDACTED] statement of medical necessity and noted that TTFT treatment was initiated for the Medicare Beneficiary on September 29, 2014, and that the Beneficiary continued to use the TTFT therapy until January 12, 2015. Appellant's representatives stated that TTFT is a non-invasive regional therapy that does not destroy other cells and helps slow cancer growth. The representatives also stated that the treatment is FDA-approved, safe, effective and exhibits minimum toxicity and resulted in better quality of life in control studies. Appellant's representatives cited many studies which showed the effectiveness of the therapy.

The Plan's representative, Dr. Dunn McGuire, stated that the health plan provides coverage according to Medicare rules. Dr. Dunn McGuire referred to the applicable LCD for E0766 which did not list any situation under which E0766 was reasonable and necessary. There were no provisions to qualify for coverage. Dr. Dunn McGuire testified that after review of the medical records from Dr. [REDACTED] the Plan maintained their original position which was to deny the pre-authorization for TTFT.

Based on the foregoing evidence in the medical record and at the hearing, the undersigned ALJ finds that there is sufficient evidence in the medical records to find TTFT (E0766) was medically reasonable and necessary in this case. While the applicable LCD states that E0766 will be denied as not reasonable and necessary, the undersigned ALJ declines to follow the LCD in this instant. Should an ALJ decline to follow a LCD, the decision must explain the reasons why the policy was not followed. *Id.* § 405.1062(b). In declining to follow the LCD, the undersigned ALJ examined the provisions in the Medicare Policy Integrity Manual regarding “reasonable and necessary.” The manual states that in making an individual determination as to whether an item or service is reasonable and necessary, contractors will analyze whether the item or service is safe and effective, and not experimental or investigational. In addition, contractors shall consider a service to be reasonable and necessary if the contractor determines that the service is:

- Safe and effective;
- Not experimental or investigational...; and
- Appropriate, including the duration and frequency that is considered appropriate for the service.

Using this as a reference, the undersigned ALJ finds that the medical records substantially document that TTFT therapy is safe and effective and not experimental or investigational in this case. As noted above, the treatment has been approved by the FDA. There are numerous clinical studies demonstrating the safety and effectiveness of the treatment. Moreover, as the medical records indicate and has been corroborated by Dr. REDACTED the TTFT treatment was appropriate for this Beneficiary given his extensive medical history, including resections, craniotomy, gamma knife treatments, recurrence and limited success with alternative treatments. It was reasonable for the physician to prescribe and initiate this treatment as it was the best FDA approved option at this time for treating recurrent atypical grade II meningioma for this Beneficiary. In addition, there is also no provision in the Plan’s Evidence of Coverage which specifically excludes TTFT treatment for recurrent atypical grade II meningioma.

Based on the foregoing evidence in the record and at the hearing, the undersigned ALJ finds that there is sufficient evidence to find that E0766 was appropriate for this Beneficiary. As the medical documents and studies show, E0766 is safe and effective, not experimental or investigational and has received FDA approval. The FDA approved the Novo TTF-100A system on April 15, 2011, for the treatment of adults with GBM that recurs or progresses after receiving chemotherapy and radiation therapy. There is sufficient documentation through controlled studies showing the effectiveness of the treatment. Although one of the studies is a Novacure funded study, other randomized studies concluded TTFT’s effectiveness. Therefore, the undersigned ALJ substantially defers to, but does not follow the applicable LCD and policy article which states that TTFT is not reasonable and necessary. Instead, the undersigned ALJ finds that TTFT was medically reasonable and necessary in this case as discussed above and finds that Humana Health Plan Inc. is required to pre-approve a tumor treatment field therapy (TTFT) device for pursuant to Medicare Part C and the Plan’s Evidence of Coverage.

CONCLUSIONS OF LAW AND ORDER

1. Humana Health Plan Inc. is required to pre-approve a tumor treatment field therapy (TTFT) device for . . . pursuant to Medicare Part C and the Plan's Evidence of Coverage.
2. The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated:

MAR 25 2020



E. M. Koldewey
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri

Appeal of:	ALJ Appeal No.: 1-7737575148
Enrollee:	Medicare Part B
HICN:	Before: David Krane U.S. Administrative Law Judge

DECISION

After careful consideration of all the evidence and arguments presented in the hearing and record, this Administrative Law Judge (“ALJ”) enters a **FULLY FAVORABLE** decision for the beneficiary, (“Beneficiary”).

Procedural History

The Beneficiary was prescribed Optune tumor treatment field therapy (“TTFT”), manufactured by NovoCure, Ltd. (“Supplier”), for treatment of glioblastoma for dates of service August 7, 2017, September 7, 2017, and October 7, 2017. At initial determination and redetermination, the Medicare Administrative Contractor (“Contractor”) with jurisdiction denied coverage. The decision was appealed and the Qualified Independent Contractor (“QIC”) issued an unfavorable reconsideration decision on June 22, 2018. (Exh. 1, pp. 1-4).

On August 2, 2018, the Office of Medicare Hearings and Appeals (“OMHA”) received the Appellant’s timely request for an ALJ Hearing. 42 C.F.R. § 405.1014(b)(1). An administrative hearing was held by telephone on October 11, 2018. The Beneficiary appeared through Debra M. Parrish, Esq., Counsel for the Beneficiary; Julie Miles, R.N., Clinical Appeals Specialist with the Supplier; and Tim Parks, R. N., Clinical Appeals Specialist with the Supplier, who observed the proceedings. The Beneficiary’s representatives testified under oath.

In the request for hearing, the Beneficiary requested consolidation of additional appeals pending for OMHA. This ALJ declines to hold a consolidated hearing on this and other pending appeals concerning the Beneficiary. It is not clear from the record that the additional appeals pending before OMHA were filed by the same appellant. 42 C.F.R. § 405.1044. Further, some of these appeals have already been assigned to other ALJs and consolidating the appeals at this point would negatively impact the orderly adjudication of appeals.

At the ALJ level of appeal, the Beneficiary submitted a position paper and a compact disc containing clinical studies, prior favorable ALJ decisions, and FDA approval letters, among other documents. Because the Beneficiary is represented by someone other than a provider or supplier, no good cause statement explaining why the evidence was not previously submitted to the QIC is required. As such, this ALJ admits the evidence as Exhibit 5. Exhibits 1 through 5 were admitted into evidence without objection and have been considered by the ALJ in reaching this decision. This ALJ carefully considered the hearing testimony, argument and record.

Issues

The issues before the ALJ include all of the issues brought out in the initial determination, coverage determination, or organization determination; redetermination; or reconsideration that were not decided entirely in a party's favor, for the claims or other appealed matters specified in the request for hearing.

Findings of Fact

After careful consideration of the entire record (Exhibit List attached and incorporated herein), a preponderance of the evidence establishes the following facts:

All jurisdictional requirements of this case have been met.

At redetermination, the Contractor explained that the Local Coverage Determination L34823 states that TTFT (E0766) will be denied as not reasonable and necessary. (Exh. 1, p. 40). The QIC determined that insufficient documentation was found in the record to quantify the effects of the device for this Beneficiary. (Exh. 1, p. 4). Additional records were not submitted to explain why this particular Beneficiary should be considered for the treatment. *Id.* Therefore, based on the documentation available, the requirements of the LCD were not met. *Id.*

The Beneficiary was a 53-year-old male on the dates of service. (Exh. 2, pp. 35-36). According to physician progress notes from February 16, 2017, the Beneficiary was diagnosed with right-frontal glioblastoma multiforme with primitive neuroendocrine tumor features in late 2011. *Id.* Resection of the tumor was completed on November 28, 2011, at Bellevue. *Id.* Chemoradiation using temozolomide in February 2012 was reported to be complicated by generalized seizure. *Id.* The February 16, 2017, progress notes indicated that the Beneficiary was then lost to follow up and later presented in December 2012 with left-sided weakness and non-paroxysmal confusion. *Id.*

An MRI performed in December 2012, showed the right frontal resection cavity and surrounding heterogeneous enhancement. (Exh. 2, pp. 35-36). In May 2013, a chest CT showed a left inguinal node that had increased in size and was mildly PET avid. *Id.* This node was excised on July 9, 2013, and showed recurrent adenocarcinoma. *Id.* On August 5, 2014, a CT of the chest, abdomen, and pelvis was clear of recurrent adenocarcinoma. *Id.* Subsequent scans performed in March 2015 and December 2015 were normal. *Id.* From January 2013, to May 2013, the Beneficiary was treated with bevacizumab and temozolomide. *Id.* Daily temozolomide treatments began in June 2013 and lasted until November 2013. *Id.* After November 2013, the

physician indicated that the Beneficiary again was lost to follow up. *Id.* The physician then noted that when the Beneficiary returned, his disease had progressed and the Beneficiary began Optune in May 2014. *Id.* According to the notes, the Beneficiary had clinical and radiographic response to the treatment. *Id.*

The physician reviewed the Beneficiary's serial MRI results. (Exh. 2, pp. 35-36). The images from July 23, 2014, and October 22, 2014, demonstrated "serially improved enhancing burden" in comparison to the image obtained on April 23, 2014, which was prior to Optune treatment. *Id.* The images obtained on February 15, 2015, May 17, 2015, October 22, 2015, February 16, 2016, and October 18, 2016, showed the Beneficiary's disease process was stable. *Id.* Imaging performed on February 16, 2017, showed the disease process had minimally evolved. *Id.* The physician indicated that the minimal radiographic changes seen did not warrant a change in treatment. *Id.* Strategies to maximize the Beneficiary's Optune compliance were discussed at the appointment. *Id.*

The report from the MRI performed on February 16, 2017, showed a small nodular focus of enhancement in the Beneficiary's left thalamus. (Exh. 2, p. 38). This area was not noted on prior imaging studies. *Id.*

An order prescribing Optune for the Beneficiary's treatment was completed on May 6, 2017, for a period of six months. (Exh. 2, p. 2). A second order was signed and completed on September 5, 2017, for continuation of therapy for an additional six months. (Exh. 2, p. 1).

Delivery documentation showed the Beneficiary received the Optune device and accessories on May 7, 2017. (Exh. 2, p. 19).

Also included in the record were multiple agreements between the Beneficiary and the Supplier. (Exh. 2, pp. 5-31). Although some of these agreements referenced an Advance Beneficiary Notice received by the Beneficiary, a copy of this notice was not found in the record.

Glioblastoma is a primary malignancy of the brain. (Exh 2, p. 141). With optimal treatment, the median survival of individuals diagnosed with glioblastoma is 15 months. *Id.* Standard treatment options include resection, chemotherapy, and radiation therapy. *Id.* Within nine months of initial treatment, most tumors recur. *Id.* Treatment options after recurrence are generally limited and include repeat resection with possible implantation of carmustine wafers, additional radiation therapy, and chemotherapy. *Id.*

Optune uses low-intensity electric fields to help slow or stop glioblastoma cancer cells from dividing.¹ Four adhesive patches, or transducer arrays, are applied to the scalp and connected to the device and a battery to deliver the therapy. *Id.* According to the Provider's instructions for the use of Optune, the treatment is intended for adult patients who are 22 years of age or older with histologically confirmed glioblastoma multiforme. (Exh. 2, p. 60). For adult patients with newly-diagnosed, supratentorial glioblastoma, Optune coupled with temozolomide is indicated following maximal debulking surgery and completion of radiation therapy along with standard of care chemotherapy. *Id.* Optune is indicated, according to the Provider's instructions, for the

¹ See <https://www.optune.com/therapy/how-therapy-works>.

treatment of recurrent glioblastoma following histologically or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. *Id.* For recurrent glioblastoma, Optune is intended to be used as a monotherapy and as an alternative to standard medical therapy for glioblastoma after surgical and radiation options have been exhausted. *Id.*

Optune, previously called NovoTTF-100A System, received FDA premarket approval for use in patients with recurrent glioblastoma on April 8, 2011.²

On October 5, 2015, the Supplier received premarket approval from the FDA for use of Optune in patients newly diagnosed with glioblastoma.³

In an article published in 2012 in *Expert Reviews Neurotherapy*, results of a phase III clinical trial for recurrent glioblastoma were discussed. *See* Fonkem E. and Wong E., NovoTTF-100A: a new treatment modality for recurrent glioblastoma, *Expert-Reviews* (2012); (Exh. 2, pp. 151-162). This article reported that TTFT “has comparable efficacy, and less toxicity, when compared to conventional drug treatments in the recurrence setting.” *Id.* The results of this clinical trial led to the FDA premarket approval for the use of the NovoTTF-100A device as monotherapy for recurrent glioblastoma.

Interim results of a later clinical trial for newly diagnosed patients showed significant improvement in outcomes of the patients, leading to crossover of trial subjects from the control group to the experimental group. On December 15, 2015, the *Journal of the American Medical Association* (“JAMA”) published an article analyzing the results of this phase III clinical trial related to TTFT.⁴ The analysis of the clinical trial showed that adding TTFT to maintenance temozolomide in a population with new onset glioblastoma “significantly prolonged progression-free and overall survival.” *Id.* After conclusion of the study, patients in the control group with ongoing maintenance therapy were offered TTFT therapy. *Id.* Thirty-five of those patients chose to receive TTFT therapy. *Id.*

The National Comprehensive Cancer Network (“NCCN”) included alternating electric field therapy for glioblastoma in its NCCN Clinical Practice Guidelines in oncology Central Nervous System Cancers guidelines version 1.2016. (Exh. 2, pp. 43-46). Use of alternating electric field therapy for recurrent glioblastoma was given a 2B rating. *Id.*

At hearing, the Beneficiary’s counsel explained the Beneficiary’s medical history and progression of the glioblastoma. (Hearing testimony). In 2011, the Beneficiary was diagnosed with glioblastoma. *Id.* He underwent conventional treatments of surgery, radiation, and chemotherapy. His conventional therapy was ended in November 2013. *Id.* After multiple rounds of treatment, disease progression was found. *Id.* At that point, the Beneficiary had exhausted other treatment options and was not eligible for resection or chemotherapy. *Id.* The Beneficiary began using the Optune device in May 2014, after which the disease was shown to

² http://www.accessdata.fda.gov/cdrh_docs/pdf10/p100034a.pdf.

³ http://www.accessdata.fda.gov/cdrh_docs/pdf10/P100034S013a.pdf.

⁴ Stupp, Roger, M.D. et al., *Maintenance Therapy With Tumor-Treating Field Plus Temozolomide vs Temozolomide Alone for Glioblastoma A Randomized Clinical Trial*, 314 JAMA 2535 (2015); (Exh. 3, pp. 1-8).

be stable. *Id.* No other treatment options were used after the Beneficiary began using Optune. *Id.* The Beneficiary continued using the Optune device through the dates of service. *Id.* For an individual diagnosed with recurrent glioblastoma, the prognosis is six months. *Id.* This Beneficiary has survived beyond that point. *Id.* After this treatment began, the Beneficiary's MRI showed no changes and the Beneficiary was clinically and radiographically stable. *Id.*

At times, patients using TTFT require a break from the therapy, which the Provider's representative stated was within the guidelines. *Id.* Patients at times can develop a rash or they are unable to tolerate the treatment every night. *Id.* It would be optimal for patient compliance to be 100%, but even with 30% compliance, clinical benefit can be seen. *Id.* Closer to 70% compliance, however, would be ideal. *Id.* This Beneficiary's success with the treatment showed compliance. *Id.*

The Optune device received FDA approval in April 2011 for use with recurrent glioblastoma. *Id.* The device exhibits minimal toxicity and provides patients with a better quality of life than other treatments. *Id.* Further, the NCCN guidelines include alternating electric field therapy for treatment of glioblastoma. *Id.* TTFT is prescribed in all fifty states, the District of Columbia, and Puerto Rico. *Id.* Finally, the Beneficiary's counsel explained that the LCD is under reconsideration at this time. *Id.*

Legal Framework

I. ALJ Review Authority

A. Jurisdiction

A party that is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services, provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. 42 C.F.R. § 405.1014; Act § 1869(b)(1)(A). In implementing this statutory directive, the Secretary has delegated the authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, unless later reviewed by the Medicare Appeals Council. *Id.*

To be considered timely, the request for hearing must be received by OMHA within sixty days after the Appellant receives the QIC's reconsideration decision. The Appellant is presumed to have received the QIC's reconsideration five days after the date noted on the first page of the reconsideration, unless there is evidence to the contrary. 42 C.F.R. § 405.1002(a)(3).

B. Scope of Review

The ALJ considers all issues not decided entirely in the Appellant's favor at any prior level of review. 42 C.F.R. § 405.1032. This ALJ may give notice to the parties if any other issue will be addressed at the hearing. *Id.* This ALJ may also issue a decision on the record on his or her own initiative if the evidence in the hearing record supports a fully favorable finding. 42 C.F.R. §§ 405.1000(g), .1038(a).

C. Standard of Review

The ALJ reviews and evaluates the evidence without regard to the findings made by the lower levels on the claim (*de novo* review). 42 C.F.R. § 405.1000(d). The Appellant bears the burden of proving each element of the Medicare claim. Sections 1814(a)(1), 1815(b), and 1833(e) of the Act; 42 C.F.R. § 424.5(a)(6), 42 C.F.R. §§ 405.1018, .1028, .1030.

II. Principles of Law

A. Statutes & Regulations

The statutory authority for the Medicare program is found in Title XVIII of the Act. *See* 42 U.S.C. § 1395 *et. seq.* The Supplementary Medical Insurance program (Part B of Title XVIII of the Act) provides coverage for a variety of medical services and supplies furnished by physicians, or by others in connection with physicians' services, for outpatient hospital services, and for a number of other specific health-related items and services. *See* Act § 1832; *see also* 42 C.F.R. § 410.10. The Secretary of HHS has authority to promulgate regulations which define or clarify the provisions of the Act. Those regulations are generally found at 42 C.F.R. § 410, and other provisions.

Notwithstanding any other provision of Title XVIII, "no payment may be made under part A or part B for any expenses incurred for items or services-which, except for items and services described in a succeeding subparagraph, are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." Act § 1862(a)(1). Custodial care expenses are also excluded from Medicare Coverage. Act § 1862(a)(9); 42 C.F.R. § 411.15(g), (k).

The Act provides that Medicare part B pays for the rental or purchase of Durable Medical Equipment, Prosthetics, Orthotics, and Supplies ("DMEPOS") if the equipment is used in the patient's home or in an institution that is used as a home. *See, e.g.,* Act §§ 1832(a)(1), (a)(2)(B), (a)(2)(I), 1834(a)(13), 1861(s)(6); 42 C.F.R. § 410.3. *See also* Act § 1861(n) (defining "durable medical equipment").

Durable medical equipment means equipment, furnished by a supplier or a home health agency that meets the following conditions:

- (1) Can withstand repeated use.
- (2) Effective with respect to items classified as DME after January 1, 2012, has an expected life of at least 3 years.

- (3) Is primarily and customarily used to serve a medical purpose.
- (4) Generally is not useful to an individual in the absence of an illness or injury.
- (5) Is appropriate for use in the home.

42 C.F.R. § 414.202.

Expenses incurred by a beneficiary for the rental or purchases of durable medical equipment (DME) are reimbursable if the following three requirements are met:

- The equipment meets the definition of DME (§110.1);
- The equipment is necessary and reasonable for the treatment of the patient's illness or injury or to improve the functioning of his or her malformed body member (§110.1); and
- The equipment is used in the patient's home.

CMS, *Medicare Benefit Policy Manual (MBPM) (Internet-Only Manual Publ'n 100-02)* ch. 15, § 110 (Oct. 2016).

In the event the services are found to be “not medically reasonable and necessary,” or “custodial in nature,” under § 1862(a)(1) or (9) of the Act, § 1879 of the Act provides for limitation on liability for Medicare payments. If the beneficiary had no knowledge that the services would not be covered, but the provider of the services did, then the provider is liable and cannot seek or retain payment by the beneficiary. The regulations at 42 C.F.R. § 411.400 *et seq.* and HCFA Ruling 95-1 address how to determine if the beneficiary or provider/supplier had the requisite degree of knowledge to make them liable under § 1879 of the Act. In general, the existence of a notice, manual, or community medical standard is sufficient to constitute notice as applicable to the provider. 42 C.F.R. § 411.406.

B. Policy and Guidance

ALJ's must give the manuals and rulings substantial deference. 42 C.F.R. § 405.1062(a). Unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than a National Coverage Determination (“NCD”), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. Act § 1871(a)(2); 42 C.F.R. § 405.1060. However, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations (“LCDs”). The applicable provisions in the LCDs and Medicare manuals are entitled to substantial deference to the extent they are consistent with the Act, regulations, and rulings; deviation from them must be explained. 42 C.F.R. § 405.1062. All relevant LCDs and Medicare manuals are hereby given substantial deference. The authority to promulgate manuals and other policy issuances is found, in part, in Section 1842 of the Act.

A Noridian Administrative Services Local Coverage Determination, LCD L34823, Tumor Treatment Field Therapy is relevant for this case. This LCD provides that tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. Noridian Healthcare Solutions, LLC, Local Coverage Determination L34823: Tumor Treatment Field Therapy (LCD L34823) (Jan. 2017). The related Policy Article states that tumor treatment field therapy devices are

covered under the Durable Medical Equipment benefit and must meet the reasonable and necessary requirements set out in the related LCD to be eligible for reimbursement. Noridian Healthcare Solutions, LLC, Local Coverage Article for Tumor Treatment Field Therapy Article A52711 (Article A52711) (Jan. 2017). The code E0766 is used to describe devices that generate electromagnetic fields utilized in the treatment of cancer. *Id.* This code is inclusive of all associated supplies. *Id.*

According to guidance contained in the Medicare Benefit Policy Manual, even though an item may be classified as DME, it may not be covered in every instance. In particular cases, coverage is subject to the requirement that the equipment be necessary and reasonable for treatment of an illness or injury, or to improve the functioning of a malformed body member. MBPM ch. 15, § 110.1.C. Additional factors to be considered are the necessity of the equipment, the reasonableness of the equipment, whether payment is consistent with what is necessary and reasonable, and establishing the period of medical necessity.

The Medicare Program Integrity Manual (CMS Pub. 100-08) (MPIM), ch. 13 § 13.5.1, and the Medicare Benefit Policy Manual (CMS Pub. 100-02) (MBPM), ch. 15 § 110, provide guidance for determining whether a device is reasonable and necessary. These manuals suggest that a device is reasonable and necessary if it is:

- Safe and effective;
- Not experimental or investigational; and
- Appropriate, including the duration and frequency that is considered appropriate for the item in terms of whether it is:
 - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;
 - Furnished in a setting appropriate to the patient's medical needs and condition;
 - Ordered and furnished by qualified personnel;
 - One that meets, but does not exceed, the patient's medical need; and
 - At least as beneficial as an existing and available medically appropriate alternative.

MPIM, ch. 13, § 13.5.1.

Medicare also instructs contractors as to the type of evidence to be used in making these technical determinations. Such decisions should be based on either "published authoritative evidence" such as "definitive randomized clinical trials" or "general acceptance by the medical community," with the caveat that "[a]cceptance by individual health care providers" and "limited case studies distributed by sponsors with a financial interest in the outcome[]" are not sufficient evidence of general acceptance by the medical community." MPIM § 13.7.1.

Equipment is necessary when it can be expected to make a meaningful contribution to the treatment of the patient's illness or injury or to the improvement of his or her malformed body member. MBPM ch. 15, § 110.1.C. In terms of reasonableness, even though an item of DME may serve a useful medical purpose, the Contractor must also consider what extent it would be reasonable for the Medicare program to pay for the item prescribed. The following are considerations in determining reasonableness:

1. Would the expense of the item to the program be clearly disproportionate to the therapeutic benefits which could ordinarily be derived from use of the equipment?
2. Is the item substantially more costly than a medically appropriate and realistically feasible alternative pattern of care?
3. Does the item serve essentially the same purpose as equipment already available to the beneficiary?

Id.

Finally, the MPIM states that LCDs which challenge the standard of practice in a community and specify that an item or service is never reasonable and necessary shall be based on sufficient evidence to **convincingly refute** evidence presented in support of coverage. *MPIM, supra* ch. 13, § 13.7.1. (emphasis added). However, “less stringent evidence is needed when allowing for individual consideration.” *Id.*

Analysis

This Administrative Law Judge conducted a *de novo* review of the evidence to determine whether the Appellant established the requirements for Medicare coverage. Appellant’s request for an ALJ hearing was timely and satisfied jurisdictional requirements. In this case, this ALJ finds and concludes that the tumor treatment field therapy for treatment of this Beneficiary’s glioblastoma for the dates of service was medically reasonable and necessary.

First, this ALJ notes that there is no National Coverage Determination specific to tumor treatment field therapy. This ALJ, therefore, looks to the relevant LCD for guidance. ALJs are not bound by LCDs and will give substantial deference to the policies if they are applicable to a particular case. 42 C.F.R. § 405.1062. If an ALJ declines to follow an LCD in a particular case, the ALJ must explain the reasons why the policy was not followed. *Id.*

In this case, this ALJ declines to follow LCD L34823 because this ALJ finds that the device is categorized as an item of durable medical equipment, which is a Medicare-covered benefit category; tumor treatment field therapy is medically reasonable and necessary to treat this Beneficiary’s condition; and no alternative treatment modalities were available to this Beneficiary.

I. Medicare-Covered Benefit Category

The Policy Article categorically places the TTFT device in the durable medical equipment category of Medicare-covered benefits. According to the relevant Policy Article, “tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act § 1861(s)(6)).” Article A52711. In fact, the Contractor provided the associated HCPCS code for the equipment and reported that the code, E0766, was in the frequent and substantial servicing payment category. Given the Contractor’s clear acceptance of the TTFT devices as items of durable medical equipment that are covered under the Medicare durable medical equipment benefit, further analysis of this issue is not necessary.

II. The TTFT is Medically Reasonable and Necessary

According to the Medicare Program Integrity Manual, contractors shall consider a service to be reasonable and necessary if the contractor determines that the service is:

- Safe and effective;
- Not experimental or investigational; and
- Appropriate, including the duration and frequency that is considered appropriate for the item or service, in terms of whether it is:
 - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;
 - Furnished in a setting appropriate to the patient's medical needs and condition;
 - Ordered and furnished by qualified personnel;
 - One that meets, but does not exceed, the patient's medical need; and
 - At least as beneficial as an existing and available medically appropriate alternative.

MPIM ch. 13, § 13.5.1.

A. Safe and Effective Therapy

Medicare does not pay for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury, or to improve the functioning of a malformed body member. Act § 1862(a)(1). To be reasonable and necessary, the procedure must be safe and effective and not experimental.

First, this ALJ finds that the Optune device received FDA premarket approval for use in patients with recurrent glioblastoma on April 8, 2011. On October 5, 2015, the FDA gave premarket approval for use of Optune in patients with newly diagnosed glioblastoma. The FDA website explains that premarket approval ("PMA") entails the following:

PMA is the most stringent type of device marketing application required by FDA. The applicant must receive FDA approval of its PMA application prior to marketing the device. PMA approval is based on a determination by FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s).⁵

While FDA premarket approval does not establish that the device is medically reasonable and necessary pursuant to Medicare requirements, it does ensure that the FDA has closely examined the device and its application. In this case, the FDA determined that sufficient scientific evidence existed to provide the FDA with assurance that the device was safe and effective for its intended use in patients with both recurrent and newly diagnosed glioblastoma. From this perspective, the use of the device meets Medicare guidance requiring that a device be proven

⁵<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm>

safe and effective based on authoritative evidence. The Contractor, however, looked to the FDA panel debate regarding the device to question the safety and effectiveness of TTFT.

In June 2014, the Contractor published responses to comments it received regarding TTFT. DME Happenings, Noridian DME Jurisdiction D, June 2014, Issue No. 43. In regard to the FDA approval of TTFT, the Contractor stated that while the FDA did approve the application with a positive vote of the FDA's Medical Device Advisory Committee's Neurological Devices Panel, the decision was split with six yes and six no on the question of whether the device was effective for use. *Id.* This vote was then decided by a tie-breaker vote cast by the panel chairperson. *Id.* While this is true, this information regarding the debate of the panel does not negate the fact that the end result of the vote was that the FDA approved the use of the device as safe and effective.

Second, this ALJ has reviewed clinical studies related to the use of the Optune device which have also concluded that the device is safe and effective. Results from a phase III clinical trial utilizing TTFT in patients with recurrent glioblastoma was shown to have equivalent efficacy when compared to the best physician's choice for chemotherapy. (Exh. 2, pp. 140-150). It is important to note that within the clinical trial, no limit was placed on the number or type of prior therapies or recurrences for the participants. *Id.* Uninterrupted treatment was recommended for the study, but breaks were permitted of up to one hour twice a day for personal care and participants were permitted to take two to three days off treatment at the end of every four weeks of treatment. *Id.* Findings from the study showed that TTFT demonstrated a "non-significant increased response rate...a trend towards reduction of the risk of death...as well as sustained improvement in [quality of life]." *Id.* Overall, TTFT was found to be at least equivalent to active chemotherapy. *Id.* However, the quality of life associated with TTFT was better than those receiving active control chemotherapy. *Id.* For instance, more gastrointestinal, hematological, and infectious events were noted in the chemotherapy group. *Id.*

With respect to patients newly diagnosed with glioblastoma, results of a phase III study released in a December 15, 2015, JAMA article showed that adding TTFT to maintenance temozolomide significantly prolonged progression-free and overall survival. (Exh. 2, pp. 48-57). Significantly, patients in the control group in the JAMA-reported study crossed over to the combined therapy group for TTFT treatment due to the improvement in outcomes seen. *Id.*

Specifically for the treatment of this Beneficiary's recurrent glioblastoma, the FDA approval and the clinical trials showed that the Optune device was safe and effective.

B. Not Experimental or Investigational

The use of TTFT is generally accepted by the medical community. In the 2016 version of the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology Central Nervous System Cancers guidelines, alternating electric field therapy is a treatment option categorized as 2B for glioblastoma. (Exh. 2, pp. 43-46). This suggestion was found in a treatment guideline from a national cancer organization, not evidence based on an individual physician treating a single patient in a clinical setting. As such, this ALJ finds that TTFT treatment is accepted in the medical community as safe and effective for the treatment of recurrent glioblastoma.

In its June 2014 response to comments on TTFT, the Contractor also addressed the NCCN guidelines. DME Happenings, Noridian DME Jurisdiction D, June 2014, Issue No. 43. Commenters suggested that NCCN category 2B showed TTFT should be covered as standard of care. The Contractor responded that NCCN category 2B means that based on “lower-level evidence, there is NCCN consensus that the intervention is appropriate.” *Id.* Category 2A means “uniform NCCN consensus that the intervention is appropriate.” *Id.* While CMS did not address NCCN guidelines as they relate to medical devices for the treatment of cancer, the Contractor referenced the Medicare Benefit Policy Manual guidance regarding NCCN evidence for off-label use of drugs and biologicals in treating cancer. *Id.* Under this MBPM guidance, the use of the drug would qualify as a medically accepted indication if the indication is a Category 1 or 2A in the NCCN. *Id.* Whereas a Category 3 indication in the NCCN would not qualify as a medically accepted indication. *Id.*

This ALJ, however, finds that referencing the MBPM guidance regarding off-label use of drugs and biologicals does not correspond to using a medical device as approved by the FDA. If a drug is being used as approved by the FDA, it is not necessary to look to Medicare-approved compendia regarding off-label uses to further determine whether the use is appropriate. Off-label, as the name suggests, indicates that the specific use contemplated was not approved by the FDA. Here, the FDA approved the use of TTFT for recurrent glioblastoma as safe and effective. Further, the MBPM did not specifically address a category 2B classification by the NCCN. The NCCN category 2B definition suggests a 2B category showed lower-level consensus that the intervention is appropriate. Generally-accepted does not mean uniformly accepted, but instead something less stringent. Here, this ALJ accepts the category 2B consensus as appropriate for this Beneficiary, particularly in light of his normally terminal diagnosis and lack of alternative treatments.

Overall, a review of the literature available showed that the Optune device received FDA premarket approval, showing that it was safe and effective and not experimental; the use of the Optune device in a population with recurrent glioblastoma was proven effective and appropriate through a phase III clinical trial; and the use of the Optune device appears in national cancer treatment guidelines for treatment of glioblastoma, showing general acceptance by the medical community.

C. The Use is Appropriate for this Beneficiary

The final question addressed in the *MPIM* is whether the item is appropriate, which the manual breaks down into multiple questions.

Here, the item was furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient’s condition. This Beneficiary had recurrent, supratentorial glioblastoma multiforme. The FDA approved the use of the Optune device in adult patients with histologically-confirmed glioblastoma multiforme, following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device was approved as a monotherapy and was intended as an alternative to standard therapy after surgical and radiation options were exhausted. As previously discussed, the Beneficiary

had exhausted all conventional therapy options, including surgery, radiation, and chemotherapy, and was using the Optune device as monotherapy for the treatment of supratentorial glioblastoma.

The device also generally is a portable device used in the patient's home or other settings, which are appropriate for this Beneficiary's medical needs and condition. The device was ordered by the Beneficiary's treating physician and the device meets, but does not exceed, the Beneficiary's medical needs. Finally, the device is at least as effective as existing and available medically appropriate alternatives. Considering that the Beneficiary had exhausted all appropriate alternative, conventional therapies, the Optune device would certainly meet this aspect of the medically reasonable and necessary considerations.

One final aspect that must be considered is whether this device is substantially more costly than a medically appropriate and realistically feasible alternative pattern of care. In a notice of intent to publish a proposed rule and soliciting comments for criteria used to make local coverage decisions, the Health Care Financing Administration (HCFA), the precursor to the Centers for Medicare and Medicaid Services, stated that it was important for the Medicare program to be responsive to the rapid advances in health care. 65 Fed. Reg. 31124, 31125 (May 16, 2000). This HCFA request for comments added that two criteria would likely be applied when making an NCD or LCD: 1. The item or service must demonstrate medical benefit, and 2. The item or service must demonstrate added value to the Medicare population. *Id.* An item was defined to be medically beneficial if it produced a "health outcome better than the natural course of illness or disease with customary medical management of symptoms." *Id.* In addition, "quality of life" was an acceptable health outcome named in the proposal. *Id.* One example provided in the notice as demonstrating added value was "when a new item or service that falls within a Medicare benefit category would be medically beneficial for a beneficiary with a given clinical circumstance and there is no Medicare-covered medically beneficial alternative." *Id.* This item or service "would add value to the program and we should cover it without consideration of costs during the coverage process." *Id.* However, for clinically substitutable services "it is not reasonable or necessary to pay for incurred costs that exceed the cost of a Medicare-covered alternative that produces the same health outcome." *Id.* Finally, if an equivalent service is "substantially more expensive than a Medicare-covered alternative" then cost considerations would lead to denial of coverage for the services. *Id.*

As reflected in the record, this Beneficiary had exhausted the conventional, alternative treatment modalities for recurrent glioblastoma. On November 28, 2011, the Beneficiary underwent resection of the tumor. (Exh. 2, p. 35). When surrounding heterogeneous enhancement was noted on MRI, resection was deferred because of callosal involvement. The Beneficiary had gone through temozolomide chemoradiation, which was complicated by generalized seizure. *Id.* He also underwent bevacizumab chemotherapy from January 2013, to May 2013, temozolomide therapy on a monthly basis from January 2013, to May 2013, and temozolomide therapy on a daily basis from June 2013, to November 2013. *Id.* Despite this treatment, the Beneficiary's disease progressed. In May 2014, after the Beneficiary had exhausted alternative treatment modalities, the Beneficiary started the use of the Optune device as monotherapy. *Id.* Since that time to the dates of service, the Beneficiary continued the use of the device. (Hearing testimony).

A review of the medical records and hearing demonstrated that this Beneficiary had already undergone surgical resection of the tumor, chemoradiation, and postradiation chemotherapy. When he began treatment with the Optune device, the Beneficiary had exhausted other treatment options and his disease continued to progress. This Beneficiary had no feasible Medicare-covered alternative pattern of care available to halt the progression of his disease. After beginning treatment, the Beneficiary's disease progression stopped, which prolonged the lifespan of the Beneficiary well beyond the general prognosis of six months for recurrent glioblastoma. The cost of this device, while high, does not outweigh the personal experience and needs of this Enrollee with respect to the TTFT device.

For the reasons stated above, this ALJ finds that Optune (TTFT) has been shown to be safe and effective and is medically reasonable and necessary for the treatment of this Enrollee's condition.

Conclusions of Law

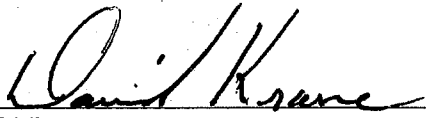
This decision is **FULLY FAVORABLE** for the Appellant. This Administrative Law Judge decides that the Optune device using tumor treatment field therapy was medically reasonable and necessary for the treatment of the Enrollee's glioblastoma for the dates of service of August 7, 2017, September 7, 2017, and October 7, 2017.

Order

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: NOV 08 2018


David Krane
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Cleveland Field Office
Cleveland, Ohio

Appeal of:

ALJ Appeal No.: **1-7819581898**

Beneficiary:

Medicare Part B

HICN:

Before: **Marc D. Lambert**
U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is issued for (hereafter Appellant).

PROCEDURAL HISTORY

Novocure (the Provider) provided the Appellant with tumor treatment field therapy services (TTFT) (E0766) from July 10, 2017, to October 10, 2017. Medicare initially denied payment for the services at issue. A Medicare redetermination upheld the denial. The redetermination was appealed to C2C Solutions, a Medicare Qualified Independent Contractor (QIC). On June 19, 2018, the QIC upheld the coverage and payment denials.

The amount in controversy meets jurisdictional requirements and the Appellant, made a timely request for an Administrative Law Judge (ALJ) hearing pursuant to 42 C.F.R. § 405.1002(a).

A telephone hearing was held on October 9, 2018, at 9:00 AM EDT in Cleveland, Ohio, before the undersigned ALJ, Debra Parrish, Esq., Outside Counsel; Julie Miles, Clinical Appeals Specialist for Novocure; and Dan McCoy, Manager of Case Management for Novocure, appeared on behalf of the Appellant. The witnesses were sworn according to law.

The case was decided pursuant to the Administrative Procedure Act (5 U.S.C. § 551 et. seq.), Title XVIII of the Social Security Act (Act), and implementing regulations and policy. The ALJ found good cause to admit additional evidence that the Appellant submitted. All remaining exhibits were admitted into evidence without objection.

ISSUES

The decisions below concluded that the TTFT services (E0766) provided to the Appellant did not meet the Medicare coverage criteria for reimbursement. The Appellant claims the services meet the Medicare coverage for reimbursement. The issue is as follows:

1. Can Medicare reimbursement be made under Part B of Title XVIII of the Act for the TTFT services (E0766) that the Provider furnished to the Appellant from July 10, 2017, to October 10, 2017?
2. If not, can the Appellant's or the Provider's liability for the TTFT services (E0766) be waived under the "waiver of liability" provisions of §1879 of the Act.

FINDINGS OF FACT

The Beneficiary was a seventy-nine (79) year old female with a diagnosis of recurrent glioblastoma multiform. (Exhibit 2, pages 1-19). The Beneficiary had been receiving TTFT therapy services since 2016. (*Id.*). The Beneficiary received continued TTFT therapy from July 10, 2017, to October 10, 2017. (*Id.*).

At the hearing, the Appellant recognized that the applicable LCD that was controlling during the date of service at issue indicated that the procedure was considered not reasonable and necessary. (*Testimony of Ms. Parrish, Hearing C.D.*). However, the Appellant argued that the ALJ should decline to follow the language of the LCD because medical studies and a consensus in the medical community show that the services are widely accepted within the medical community. (*Id.*). The Appellant also argued that the Beneficiary continues to benefit from TTFT. (*Id.*).

In support of its argument, the Appellant submitted multiple peer reviewed studies on the benefits of TTFT therapy. (Exhibit 2, pages 1-61). At the hearing, the Appellant also explained that the Medicare Contractor is currently reconsidering their LCD on TTFT therapy. (*Testimony of Ms. Parrish, Hearing C.D.*).

LEGAL FRAMEWORK

I. ALJ Review Authority

Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. (§ 1869(b)(1)(A) of the Act).

In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. (*See* 70 Fed.

Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. (*Id.*).

A hearing before an ALJ is only available if the remaining amount in controversy meets the minimum requirement. 42 C.F.R. §405.1006. The request for hearing is timely if filed within sixty (60) days after receipt of a QIC reconsideration decision. *See* 42 C.F.R. § 405.1014.

B. Scope of Review

Under the Centers for Medicare and Medicaid Services' (CMS) implementation policy for the Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 (BIPA), Pub. Law 106-554, app. F, 114 Stat. 2763, 2763A-463, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), Pub. Law 108-173, 117 Stat. 2066, all Medicare Part A and Part B claims, which have been issued a redetermination by a Fiscal Intermediary (FI) on or after May 1, 2005, and all Medicare Part B claims, which have been issued a redetermination by a Carrier on or after January 1, 2006, are governed by the ALJ hearing procedures outlined at 42 C.F.R. § 405.1000 through § 405.1054. *See* 70 Fed. Reg. 11420, 11424-26 (Mar. 8, 2005).

"The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in a party's favor. (For purposes of this provision, the term "party" does not include a representative of CMS or one of its contractors that may be participating in the hearing.) However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, he or she notifies the parties before the hearing and may consider it an issue at the hearing." 42 C.F.R. § 405.1032(a).

"An ALJ may also issue a decision on the record on his or her own initiative if the evidence in the hearing record supports a fully favorable finding." *See* 42 C.F.R. §§ 405.1000(g) and (e) and .1038(a). In addition, "[i]f all parties to the hearing waive their right to appear at the hearing in person or by telephone or video-teleconference, the ALJ may make a decision based on the evidence that is in the file and any new evidence that is submitted for consideration." 42 C.F.R. § 405.1000(e).

C. Standard of Review

"The ALJ conducts a de novo review and issues a decision based on the hearing record." (42 C.F.R. § 405.1000(f)).

II. Principles of Law

A. Statutes and Regulations

Part B of Title XVIII of the Social Security Act, the Supplementary Medical Insurance program, provides coverage for a variety of medical services and supplies furnished by physicians, or by others in connection with physicians' services, for outpatient hospital services, and for a number of other specific health-related items and services. Individuals participate voluntarily in the Medicare Part B program and pay a monthly premium.

Section 1862(a)(1) of the Social Security Act excludes Medicare payment for services which "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

Section 1832(a) of the Act states, in pertinent part: The benefits provided to an individual by the insurance program established by this part shall consist of

- (1) entitlement to have payment made to him or on his behalf (subject to the provisions of this part) for medical or other health services...

Pursuant to 42 C.F.R. § 410.20(a) and (b), Medicare Part B pays for physicians' services, including diagnosis, therapy, surgery, consultations, and home, office, and institutional calls, when furnished by qualified professionals.

Section 1833(e) of the Act states that "[n]o payment shall be made to any provider of services or other person under this part unless there has been furnished such information as may be necessary in order to determine the amounts due such provider or other person under this part for the period with respect to which the amounts are being paid or for any prior period." It is expected the patient's medical records will reflect the need for the care provided, and include, but are not limited to, physician's office records, hospital records, and test reports. The Regulations place the burden on the appropriate party – either the provider, supplier, or beneficiary, to furnish "sufficient information" to determine whether payment is due and the amount of payment. 42 C.F.R. § 424.5(a)(6). Without pertinent documentation, there is no objective means of making a "reasonable and necessary" determination as required by § 1862(a)(1)(A) of the Act.

Section 1879(a) of the Act provides that if the services provided are deemed to be not reasonable and necessary for the diagnosis and treatment of an illness or injury or to improve the functioning of a malformed body member or are deemed to be custodial, payment under Part B may still be made if both the Beneficiary and the Provider of the services did not know, nor reasonably should have been expected to know, that the services would not be reimbursable by Medicare. If no payment may be made under this section, the Beneficiary's liability for the charges incurred may be waived if the Beneficiary did not know, nor reasonably should have been expected to know, that the services would not be reimbursable by Medicare. (§ 1879(b)).

B. Policy and Guidance

"The primary authority for all coverage provisions and subsequent policies is the Social Security Act (the Act). Contractors use Medicare policies in the form of regulations, NCDs [*national coverage determinations*], coverage provisions in interpretive manuals, and LCDs [*local coverage determinations*] to apply the provisions of the Act." Medicare Program Integrity Manual (MPIM) (Internet-Only Manual Publ'n 100-08) ch. 13, § 13.1 (May 2004). Section 1871(a)(2) of the Act provides that unless promulgated as a regulation by The Centers for Medicare and Medicaid Services (CMS), no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.1060. The CMS administers the Medicare Program (Act §§ 1102, 1871, and

1874) and contracts with carriers and intermediaries (Medicare contractors) to act on its behalf in determining and making payments to providers and suppliers of Medicare items and services. Act §§ 1816 and 1842. In lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (LMRPs) or local coverage determinations (LCDs). Medicare contractors issue written determinations, called LCDs, specifying under what clinical circumstances a service is considered to be reasonable and necessary. They are administrative and educational tools to assist providers in submitting correct claims for payment. MPIM, *Id.*, § 13.1.3. Contractors publish LCDs to provide guidance to the public and medical community within their jurisdictions whether, on a contractor-wide basis, a particular item or service is covered. Act, § 1869(f)(2)(B). LCDs are used only on a contractor-wide basis and may differ between contractors in different regions of the country.

An ALJ is not bound by LCDs, LMRPs, or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. See 42 C.F.R. § 405.1062(a). If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. See 42 C.F.R. § 405.1062(b).

In the CMS, Medicare National Coverage Determinations Manual ("MNCDM") (Internet-Only Manual Publ'n 100-03) ch. 1 (May 2005), CMS "describes whether specific medical items, services, treatment procedures, or technologies can be paid for under Medicare. National coverage decisions have been made on the items addressed in this manual. All decisions that items, services, etc. are not covered are based on § 1862(a)(1) of the Act (the "not reasonable and necessary" exclusion) unless otherwise specifically noted." *Id.*, Part 1, Foreword. National Coverage Determinations (NCDs) made under § 1862(a)(1) of the Act are binding on ALJs during the claim appeal process. See 42 C.F.R. § 405.1060.

For the period of time relevant to this case, the Medicare Contractor, CGS, issued a medical policy titled LCD for Tumor Treatment Field Therapy (TTFT) (L34823), which indicated that TTFT services were not reasonable and necessary during the date of service at issue.

Analysis

The QIC upheld the denial, finding the documentation did not support the TTFT services (E0766) were reasonable and necessary. The Appellant contends that Medicare coverage and reimbursement is warranted in this case. Careful consideration of the entire record and applicable law supports the ALJ's determination that the procedure at issue warrants coverage under Medicare Part B.

Initially, the ALJ notes the LCD for Tumor Treatment Field Therapy (TTFT) (L34823), which was controlling during the dates of service at issue, indicates TTFT services are not reasonable and necessary. However, after careful consideration of the evidence included in the record and the testimony presented at the hearing, the ALJ declines to follow the language of the LCD because the evidence supports the procedure was reasonable and necessary for the Beneficiary during the

date of service at issue. Significantly, the Appellant submitted numerous peer reviewed medical studies, statements from physicians and professional societies, and insurance coverage policies, all of which show the procedure was accepted as a safe and effective medical procedure. Moreover, the ALJ is persuaded by the fact that the Beneficiary had been benefiting from TFFT reflects that the services were reasonable and necessary in this case. After careful consideration of all the evidence in the record, the ALJ declines to follow the LCD and finds that TFFT services at issue are reasonable and necessary. Accordingly, the ALJ finds the TFFT services (E0766) at issue meets Medicare criteria for reimbursement.

CONCLUSIONS OF LAW

The Appellant satisfied the applicable coverage criteria for reimbursement under Part B of the Act for the TFFT services (E0766) that it furnished to the Beneficiary from July 10, 2017, to October 10, 2017. Therefore, as a matter of law, the TFFT services (E0766) furnished on the above date was reasonable and necessary under § 1862(a) of the Act, and the documentation requirements of § 1833(e) were sufficiently satisfied for Medicare to provide reimbursement.

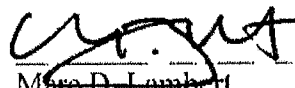
ORDER

For the reasons discussed above the Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Date

10/13/18



Marc D. Lambert

U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Cleveland Field Office
Cleveland, Ohio

Appeal of:

ALJ Appeal No.: 1-7737574789

Beneficiary:

Medicare Part B

HICN:

Before: **Marc D. Lambert**
U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is issued for [hereafter Appellant).

PROCEDURAL HISTORY

Novocure (the Provider) provided the Appellant with tumor treatment field therapy services (TTFT) (E0766) from August 3, 2017, to November 3, 2017. Medicare initially denied payment for the services at issue. A Medicare redetermination upheld the denial. The redetermination was appealed to C2C Solutions, a Medicare Qualified Independent Contractor (QIC). On June 19, 2018, the QIC upheld the coverage and payment denials.

The amount in controversy meets jurisdictional requirements and the Appellant, made a timely request for an Administrative Law Judge (ALJ) hearing pursuant to 42 C.F.R. § 405.1002(a).

A telephone hearing was held on October 2, 2018, at 11:00 AM EDT in Cleveland, Ohio, before the undersigned ALJ, Debra Parrish, Esq., Outside Counsel; Julie Miles, Clinical Appeals Specialist for Novocure; and Dan McCoy, Manager of Case Management for Novocure, appeared on behalf of the Appellant. The witnesses were sworn according to law.

The case was decided pursuant to the Administrative Procedure Act (5 U.S.C. § 551 et. seq.), Title XVIII of the Social Security Act (Act), and implementing regulations and policy. The ALJ found good cause to admit additional evidence that the Appellant submitted. All remaining exhibits were admitted into evidence without objection.

ISSUES

The decisions below concluded that the TTFT services (E0766) provided to the Appellant did not meet the Medicare coverage criteria for reimbursement. The Appellant claims the services meet the Medicare coverage for reimbursement. The issue is as follows:

1. Can Medicare reimbursement be made under Part B of Title XVIII of the Act for the TTFT services (E0766) that the Provider furnished to the Appellant from August 3, 2017, to November 3, 2017?
2. If not, can the Appellant's or the Provider's liability for the TTFT services (E0766) be waived under the "waiver of liability" provisions of §1879 of the Act.

FINDINGS OF FACT

The Beneficiary is a sixty-nine (69) year old female with a diagnosis of recurrent glioblastoma multiform. (Exhibit 2, pages 1-19). The Beneficiary had been receiving TTFT therapy services since 2016. (*Id.*). The Beneficiary received continued TTFT therapy from August 3, 2017, to November 3, 2017. (*Id.*).

At the hearing, the Appellant recognized that the applicable LCD that was controlling during the date of service at issue indicated that the procedure was considered not reasonable and necessary. (*Testimony of Ms. Parrish*, Hearing C.D.). However, the Appellant argued that the ALJ should decline to follow the language of the LCD because medical studies and a consensus in the medical community show that the services are widely accepted within the medical community. (*Id.*). The Appellant also argued that the Beneficiary is alive after two (2) years of TTFT therapy, which is unusual for patients with recurrent glioblastoma. (*Testimony of Ms. Miles*, Hearing C.D.).

In support of its argument, the Appellant submitted multiple peer reviewed studies on the benefits of TTFT therapy. (*Id.*). At the hearing, the Appellant also explained that the Medicare Contractor is currently reconsidering their LCD on TTFT therapy. (*Testimony of Ms. Parrish*, Hearing C.D.).

LEGAL FRAMEWORK

I. ALJ Review Authority

Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. (§ 1869(b)(1)(A) of the Act).

In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. (*See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. (*Id.*).

A hearing before an ALJ is only available if the remaining amount in controversy meets the minimum requirement. 42 CFR §405.1006. The request for hearing is timely if filed within sixty (60) days after receipt of a QIC reconsideration decision. *See* 42 C.F.R. § 405.1014.

B. Scope of Review

Under the Centers for Medicare and Medicaid Services' (CMS) implementation policy for the Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 (BIPA), Pub. Law 106-554, app. F, 114 Stat. 2763, 2763A-463, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), Pub. Law 108-173, 117 Stat. 2066, all Medicare Part A and Part B claims, which have been issued a redetermination by a Fiscal Intermediary (FI) on or after May 1, 2005, and all Medicare Part B claims, which have been issued a redetermination by a Carrier on or after January 1, 2006, are governed by the ALJ hearing procedures outlined at 42 C.F.R. § 405.1000 through § 405.1054. *See* 70 Fed. Reg. 11420, 11424-26 (Mar. 8, 2005).

"The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in a party's favor. (For purposes of this provision, the term "party" does not include a representative of CMS or one of its contractors that may be participating in the hearing.) However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, he or she notifies the parties before the hearing and may consider it an issue at the hearing." 42 C.F.R. § 405.1032(a).

"An ALJ may also issue a decision on the record on his or her own initiative if the evidence in the hearing record supports a fully favorable finding." *See* 42 C.F.R. §§ 405.1000(g) and (c) and .1038(a). In addition, "[i]f all parties to the hearing waive their right to appear at the hearing in person or by telephone or video-teleconference, the ALJ may make a decision based on the evidence that is in the file and any new evidence that is submitted for consideration." 42 C.F.R. § 405.1000(c).

C. Standard of Review

"The ALJ conducts a de novo review and issues a decision based on the hearing record." (42 C.F.R. § 405.1000(i)).

II. Principles of Law

A. Statutes and Regulations

Part B of Title XVIII of the Social Security Act, the Supplementary Medical Insurance program, provides coverage for a variety of medical services and supplies furnished by physicians, or by others in connection with physicians' services, for outpatient hospital services, and for a number

of other specific health-related items and services. Individuals participate voluntarily in the Medicare Part B program and pay a monthly premium.

Section 1862(a)(1) of the Social Security Act excludes Medicare payment for services which "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

Section 1832(a) of the Act states, in pertinent part: The benefits provided to an individual by the insurance program established by this part shall consist of

- (1) entitlement to have payment made to him or on his behalf (subject to the provisions of this part) for medical or other health services...

Pursuant to 42 C.F.R. § 410.20(a) and (b), Medicare Part B pays for physicians' services, including diagnosis, therapy, surgery, consultations, and home, office, and institutional calls, when furnished by qualified professionals.

Section 1833(c) of the Act states that "[n]o payment shall be made to any provider of services or other person under this part unless there has been furnished such information as may be necessary in order to determine the amounts due such provider or other person under this part for the period with respect to which the amounts are being paid or for any prior period." It is expected the patient's medical records will reflect the need for the care provided, and include, but are not limited to, physician's office records, hospital records, and test reports. The Regulations place the burden on the appropriate party – either the provider, supplier, or beneficiary, to furnish "sufficient information" to determine whether payment is due and the amount of payment. 42 C.F.R. § 424.5(a)(6). Without pertinent documentation, there is no objective means of making a "reasonable and necessary" determination as required by § 1862(a)(1)(A) of the Act.

Section 1879(a) of the Act provides that if the services provided are deemed to be not reasonable and necessary for the diagnosis and treatment of an illness or injury or to improve the functioning of a malformed body member or are deemed to be custodial, payment under Part B may still be made if both the Beneficiary and the Provider of the services did not know, nor reasonably should have been expected to know, that the services would not be reimbursable by Medicare. If no payment may be made under this section, the Beneficiary's liability for the charges incurred may be waived if the Beneficiary did not know, nor reasonably should have been expected to know, that the services would not be reimbursable by Medicare. (§ 1879(b)).

B. Policy and Guidance

"The primary authority for all coverage provisions and subsequent policies is the Social Security Act (the Act). Contractors use Medicare policies in the form of regulations, NCDs [*national coverage determinations*], coverage provisions in interpretive manuals, and LCDs [*local coverage determinations*] to apply the provisions of the Act." Medicare Program Integrity Manual (MPIM) (Internet-Only Manual Pub'n 100-08) ch. 13, § 13.1 (May 2004). Section 1871(a)(2) of the Act provides that unless promulgated as a regulation by The Centers for Medicare and Medicaid Services (CMS), no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard

governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.1060. The CMS administers the Medicare Program (Act §§ 1102, 1871, and 1874) and contracts with carriers and intermediaries (Medicare contractors) to act on its behalf in determining and making payments to providers and suppliers of Medicare items and services. Act §§ 1816 and 1842. In lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (LMRPs) or local coverage determinations (LCDs). Medicare contractors issue written determinations, called LCDs, specifying under what clinical circumstances a service is considered to be reasonable and necessary. They are administrative and educational tools to assist providers in submitting correct claims for payment. MPIM, *Id.*, § 13.1.3. Contractors publish LCDs to provide guidance to the public and medical community within their jurisdictions whether, on a contractor-wide basis, a particular item or service is covered. Act, § 1869(f)(2)(B). LCDs are used only on a contractor-wide basis and may differ between contractors in different regions of the country.

An ALJ is not bound by LCDs, LMRPs, or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. *See* 42 C.F.R. § 405.1062(a). If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. *See* 42 C.F.R. § 405.1062(b).

In the CMS, Medicare National Coverage Determinations Manual ("MNCDM") (Internet-Only Manual Publ'n 100-03) ch. 1 (May 2005), CMS "describes whether specific medical items, services, treatment procedures, or technologies can be paid for under Medicare. National coverage decisions have been made on the items addressed in this manual. All decisions that items, services, etc. are not covered are based on § 1862(a)(1) of the Act (the "not reasonable and necessary" exclusion) unless otherwise specifically noted." *Id.*, Part 1. Foreword. National Coverage Determinations (NCDs) made under § 1862(a)(1) of the Act are binding on ALJs during the claim appeal process. *See* 42 C.F.R. § 405.1060.

For the period of time relevant to this case, the Medicare Contractor, Noridian Healthcare Solutions, issued a medical policy titled LCD for Tumor Treatment Field Therapy (TTFT) (L34823), which indicated that TTFT services were not reasonable and necessary during the date of service at issue.

Analysis

The QIC upheld the denial, finding the documentation did not support the TTFT services (L0766) were reasonable and necessary. The Appellant contends that Medicare coverage and reimbursement is warranted in this case. Careful consideration of the entire record and applicable law supports the ALJ's determination that the procedure at issue warrants coverage under Medicare Part B.

Initially, the ALJ notes the LCD for Tumor Treatment Field Therapy (TTFT) (L34823), which was controlling during the dates of service at issue, indicates TTFT services are not reasonable and

necessary. However, after careful consideration of the evidence included in the record and the testimony presented at the hearing, the ALJ declines to follow the language of the LCD because the evidence supports the procedure was reasonable and necessary for the Beneficiary during the date of service at issue. Significantly, the Appellant submitted numerous peer reviewed medical studies, statements from physicians and professional societies, and insurance coverage policies, all of which show the procedure was accepted as a safe and effective medical procedure. Moreover, the ALJ is persuaded by the fact that the Beneficiary had been benefiting from TTFT for over two years reflects that the services were reasonable and necessary in this case. Accordingly, after careful consideration of all the evidence in the record, the ALJ declines to follow the LCD and finds that TTFT services at issue are reasonable and necessary. Accordingly, the ALJ finds the TFT services (E0766) at issue meets Medicare criteria for reimbursement.

CONCLUSIONS OF LAW

The Appellant satisfied the applicable coverage criteria for reimbursement under Part B of the Act for the TTFT services (E0766) that it furnished to the Beneficiary from August 3, 2017, to November 3, 2017. Therefore, as a matter of law, the TTFT services (E0766) furnished on the above date was reasonable and necessary under § 1862(a) of the Act, and the documentation requirements of § 1833(e) were sufficiently satisfied for Medicare to provide reimbursement.


ORDER

For the reasons discussed above the Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

10/15/18

Date



Marc D. Lambert
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Cleveland Field Office
Cleveland, Ohio

Appeal of:

ALJ Appeal No.: **1-7958692254**

Beneficiary:

Medicare Part B

HICN:

Before: **Marc D. Lambert**
U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is issued for (hereafter Appellant).

PROCEDURAL HISTORY

Novocure (the Provider) provided the Appellant with tumor treatment field therapy services (TTFT) (E0766) from December 8, 2017, to February 8, 2018. Medicare initially denied payment for the services at issue. A Medicare redetermination upheld the denial. The redetermination was appealed to C2C Solutions, a Medicare Qualified Independent Contractor (QIC). On June 19, 2018, the QIC upheld the coverage and payment denials.

The amount in controversy meets jurisdictional requirements and the Appellant, made a timely request for an Administrative Law Judge (ALJ) hearing pursuant to 42 C.F.R. § 405.1002(a).

Although the Appellant requested a hearing, this decision is being issued in the absence of a hearing as a review of the evidence in the record warrants a fully favorable finding in favor of the Appellant on every issue, in compliance with 42 C.F.R. § 405.1038(a).

The case was decided pursuant to the Administrative Procedure Act (5 U.S.C. § 551 et. seq.), Title XVIII of the Social Security Act (Act), and implementing regulations and policy. The ALJ found good cause to admit additional evidence that the Appellant submitted. All remaining exhibits were admitted into evidence without objection.

ISSUES

The decisions below concluded that the TTFT services (E0766) provided to the Appellant did not meet the Medicare coverage criteria for reimbursement. The Appellant claims the services meet the Medicare coverage for reimbursement. The issue is as follows:

1. Can Medicare reimbursement be made under Part B of Title XVIII of the Act for the TTFT services (E0766) that the Provider furnished to the Appellant from December 8, 2017, to February 8, 2018?
2. If not, can the Appellant's or the Provider's liability for the TTFT services (E0766) be waived under the "waiver of liability" provisions of §1879 of the Act.

FINDINGS OF FACT

The Beneficiary is an eighty-four (84) year old female with a diagnosis of recurrent glioblastoma multiform. (Exhibit 2, pages 1-206). The Beneficiary received TTFT therapy from December 8, 2017, to February 8, 2018. (*Id.*).

Through its Request for Hearing, the Appellant recognized that the applicable LCD that was controlling during the date of service at issue indicated that the procedure was considered not reasonable and necessary. (Exhibit 1). However, the Appellant argued that the ALJ should decline to follow the language of the LCD because medical studies and a consensus in the medical community show that the services are widely accepted within the medical community. (*Id.*). In support of its argument, the Appellant submitted multiple peer reviewed studies on the benefits of TTFT therapy. (Exhibit 2, pages 1-206).

LEGAL FRAMEWORK

I. ALJ Review Authority

Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. (§ 1869(b)(1)(A) of the Act).

In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. (*See* 70 Fed. Reg. 36386, 36387 (June 23, 2005)). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. (*Id.*).

A hearing before an ALJ is only available if the remaining amount in controversy meets the minimum requirement. 42 CFR §405.1006. The request for hearing is timely if filed within sixty (60) days after receipt of a QIC reconsideration decision. *See* 42 C.F.R. § 405.1014.

B. Scope of Review

Under the Centers for Medicare and Medicaid Services' (CMS) implementation policy for the Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 (BIPA), Pub. Law 106-554, app. F, 114 Stat. 2763, 2763A-463, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), Pub. Law 108-173, 117 Stat. 2066, all Medicare Part A and Part B claims, which have been issued a redetermination by a Fiscal Intermediary (FI) on or after May 1, 2005, and all Medicare Part B claims, which have been issued a redetermination by a Carrier on or after January 1, 2006, are governed by the ALJ hearing procedures outlined at 42 C.F.R. § 405.1000 through § 405.1054. *See* 70 Fed. Reg. 11420, 11424-26 (Mar. 8, 2005).

"The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in a party's favor. (For purposes of this provision, the term "party" does not include a representative of CMS or one of its contractors that may be participating in the hearing.) However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, he or she notifies the parties before the hearing and may consider it an issue at the hearing." 42 C.F.R. § 405.1032(a).

"An ALJ may also issue a decision on the record on his or her own initiative if the evidence in the hearing record supports a fully favorable finding." *See* 42 C.F.R. §§ 405.1000(g) and (e) and .1038(a). In addition, "[i]f all parties to the hearing waive their right to appear at the hearing in person or by telephone or video-teleconference, the ALJ may make a decision based on the evidence that is in the file and any new evidence that is submitted for consideration." 42 C.F.R. § 405.1000(e).

C. Standard of Review

"The ALJ conducts a de novo review and issues a decision based on the hearing record." (42 C.F.R. § 405.1000(f)).

II. Principles of Law

A. Statutes and Regulations

Part B of Title XVIII of the Social Security Act, the Supplementary Medical Insurance program, provides coverage for a variety of medical services and supplies furnished by physicians, or by others in connection with physicians' services, for outpatient hospital services, and for a number of other specific health-related items and services. Individuals participate voluntarily in the Medicare Part B program and pay a monthly premium.

Section 1862(a)(1) of the Social Security Act excludes Medicare payment for services which "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

Section 1832(a) of the Act states, in pertinent part: The benefits provided to an individual by the insurance program established by this part shall consist of

- (1) entitlement to have payment made to him or on his behalf (subject to the provisions of this part) for medical or other health services...

Pursuant to 42 C.F.R. § 410.20(a) and (b), Medicare Part B pays for physicians' services, including diagnosis, therapy, surgery, consultations, and home, office, and institutional calls, when furnished by qualified professionals.

Section 1833(e) of the Act states that "[n]o payment shall be made to any provider of services or other person under this part unless there has been furnished such information as may be necessary in order to determine the amounts due such provider or other person under this part for the period with respect to which the amounts are being paid or for any prior period." It is expected the patient's medical records will reflect the need for the care provided, and include, but are not limited to, physician's office records, hospital records, and test reports. The Regulations place the burden on the appropriate party – either the provider, supplier, or beneficiary, to furnish "sufficient information" to determine whether payment is due and the amount of payment. 42 C.F.R. § 424.5(a)(6). Without pertinent documentation, there is no objective means of making a "reasonable and necessary" determination as required by § 1862(a)(1)(A) of the Act.

Section 1879(a) of the Act provides that if the services provided are deemed to be not reasonable and necessary for the diagnosis and treatment of an illness or injury or to improve the functioning of a malformed body member or are deemed to be custodial, payment under Part B may still be made if both the Beneficiary and the Provider of the services did not know, nor reasonably should have been expected to know, that the services would not be reimbursable by Medicare. If no payment may be made under this section, the Beneficiary's liability for the charges incurred may be waived if the Beneficiary did not know, nor reasonably should have been expected to know, that the services would not be reimbursable by Medicare. (§ 1879(b)).

B. Policy and Guidance

"The primary authority for all coverage provisions and subsequent policies is the Social Security Act (the Act). Contractors use Medicare policies in the form of regulations, NCDs [*national coverage determinations*], coverage provisions in interpretive manuals, and LCDs [*local coverage determinations*] to apply the provisions of the Act." Medicare Program Integrity Manual (MPIM) (Internet-Only Manual Publ'n 100-08) ch. 13, § 13.1 (May 2004). Section 1871(a)(2) of the Act provides that unless promulgated as a regulation by The Centers for Medicare and Medicaid Services (CMS), no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.1060. The CMS administers the Medicare Program (Act §§ 1102, 1871, and 1874) and contracts with carriers and intermediaries (Medicare contractors) to act on its behalf in

determining and making payments to providers and suppliers of Medicare items and services. Act §§ 1816 and 1842. In lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (LMRPs) or local coverage determinations (LCDs). Medicare contractors issue written determinations, called LCDs, specifying under what clinical circumstances a service is considered to be reasonable and necessary. They are administrative and educational tools to assist providers in submitting correct claims for payment. MPIM, *Id.*, § 13.1.3. Contractors publish LCDs to provide guidance to the public and medical community within their jurisdictions whether, on a contractor-wide basis, a particular item or service is covered. Act, § 1869(f)(2)(B). LCDs are used only on a contractor-wide basis and may differ between contractors in different regions of the country.

An ALJ is not bound by LCDs, LMRPs, or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. See 42 C.F.R. § 405.1062(a). If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. See 42 C.F.R. § 405.1062(b).

In the CMS, Medicare National Coverage Determinations Manual ("MNCDM") (Internet-Only Manual Publ'n 100-03) ch. 1 (May 2005), CMS "describes whether specific medical items, services, treatment procedures, or technologies can be paid for under Medicare. National coverage decisions have been made on the items addressed in this manual. All decisions that items, services, etc. are not covered are based on § 1862(a)(1) of the Act (the "not reasonable and necessary" exclusion) unless otherwise specifically noted." *Id.*, Part 1, Foreword. National Coverage Determinations (NCDs) made under § 1862(a)(1) of the Act are binding on ALJs during the claim appeal process. See 42 C.F.R. § 405.1060.

For the period of time relevant to this case, the Medicare Contractor, Noridian Healthcare Solutions, issued a medical policy titled LCD for Tumor Treatment Field Therapy (TTFT) (L34823), which indicated that TTFT services were not reasonable and necessary during the date of service at issue.

Analysis

The QIC upheld the denial, finding the documentation did not support the TTFT services (E0766) were reasonable and necessary. The Appellant contends that Medicare coverage and reimbursement is warranted in this case. Careful consideration of the entire record and applicable law supports the ALJ's determination that the procedure at issue warrants coverage under Medicare Part B.

Initially, the ALJ notes the LCD for Tumor Treatment Field Therapy (TTFT) (L34823), which was controlling during the dates of service at issue, indicates TTFT services are not reasonable and necessary. However, after careful consideration of the evidence included in the record, the ALJ declines to follow the language of the LCD because the evidence supports the procedure was reasonable and necessary for the Beneficiary during the date of service at issue. Significantly, the

Appellant submitted numerous peer reviewed medical studies, statements from physicians and professional societies, and insurance coverage policies, all of which show the procedure was accepted as a safe and effective medical procedure. Moreover, the ALJ is persuaded by the fact that the Beneficiary is benefiting from TTFT. Accordingly, after careful consideration of all the evidence in the record, the ALJ declines to follow the LCD and finds that TTFT services at issue are reasonable and necessary. Accordingly, the ALJ finds the TTF services (E0766) at issue meets Medicare criteria for reimbursement.

CONCLUSIONS OF LAW

The Appellant satisfied the applicable coverage criteria for reimbursement under Part B of the Act for the TTFT services (E0766) that it furnished to the Beneficiary from December 8, 2017, to February 8, 2018. Therefore, as a matter of law, the TTFT services (E0766) furnished on the above date was reasonable and necessary under § 1862(a) of the Act, and the documentation requirements of § 1833(e) were sufficiently satisfied for Medicare to provide reimbursement.


ORDER

For the reasons discussed above the Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

OCT 25 2018

Date



Marc D. Lambert

U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Cleveland Field Office
Cleveland, Ohio

Appeal of:	ALJ Appeal No.: 1-7904952491
Beneficiary:	Medicare Part B
HICN:	Before: Marc D. Lambert U.S. Administrative Law Judge

DECISION

After careful consideration of the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is issued for (hereafter Appellant).

PROCEDURAL HISTORY

Novocure (the Provider) provided the Appellant with tumor treatment field therapy services (TTFT) (E0766) from November 8, 2017, to January 8, 2018. Medicare initially denied payment for the services at issue. A Medicare redetermination upheld the denial. The redetermination was appealed to C2C Solutions, a Medicare Qualified Independent Contractor (QIC). On August 17, 2018, the QIC upheld the coverage and payment denials.

The amount in controversy meets jurisdictional requirements and the Appellant, made a timely request for an Administrative Law Judge (ALJ) hearing pursuant to 42 C.F.R. § 405.1002(a).

Although the Appellant requested a hearing, this decision is being issued in the absence of a hearing as a review of the evidence in the record warrants a fully favorable finding in favor of the Appellant on every issue, in compliance with 42 C.F.R. § 405.1038(a).

The case was decided pursuant to the Administrative Procedure Act (5 U.S.C. § 551 et. seq.), Title XVIII of the Social Security Act (Act), and implementing regulations and policy. The ALJ found good cause to admit additional evidence that the Appellant submitted. All remaining exhibits were admitted into evidence without objection.

ISSUES

The decisions below concluded that the TTFT services (E0766) provided to the Appellant did not meet the Medicare coverage criteria for reimbursement. The Appellant claims the services meet the Medicare coverage for reimbursement. The issue is as follows:

1. Can Medicare reimbursement be made under Part B of Title XVIII of the Act for the TTFT services (E0766) that the Provider furnished to the Appellant from November 8, 2017, to January 8, 2018?
2. If not, can the Appellant's or the Provider's liability for the TTFT services (E0766) be waived under the "waiver of liability" provisions of §1879 of the Act.

FINDINGS OF FACT

The Beneficiary is a sixty-one (61) year old female with a diagnosis of recurrent glioblastoma multiform. (Exhibit 2, pages 1-32). The Beneficiary received TTFT therapy from November 8, 2017, to January 8, 2018. (*Id.*).

Through its Request for Hearing, the Appellant recognized that the applicable LCD that was controlling during the date of service at issue indicated that the procedure was considered not reasonable and necessary. (Exhibit 1). However, the Appellant argued that the ALJ should decline to follow the language of the LCD because medical studies and a consensus in the medical community show that the services are widely accepted within the medical community. (*Id.*). In support of its argument, the Appellant submitted multiple peer reviewed studies on the benefits of TTFT therapy. (Exhibit 3).

LEGAL FRAMEWORK

I. ALJ Review Authority

Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (HHS), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. (§ 1869(b)(1)(A) of the Act).

In implementing this statutory directive, the Secretary has delegated his authority to administer the nationwide hearings and appeals system for the Medicare program to OMHA. (*See* 70 Fed. Reg. 36386, 36387 (June 23, 2005). The ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. (*Id.*).

A hearing before an ALJ is only available if the remaining amount in controversy meets the minimum requirement. 42 CFR §405.1006. The request for hearing is timely if filed within sixty (60) days after receipt of a QIC reconsideration decision. See 42 C.F.R. § 405.1014.

B. Scope of Review

Under the Centers for Medicare and Medicaid Services' (CMS) implementation policy for the Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000 (BIPA), Pub. Law 106-554, app. F, 114 Stat. 2763, 2763A-463, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), Pub. Law 108-173, 117 Stat. 2066, all Medicare Part A and Part B claims, which have been issued a redetermination by a Fiscal Intermediary (FI) on or after May 1, 2005, and all Medicare Part B claims, which have been issued a redetermination by a Carrier on or after January 1, 2006, are governed by the ALJ hearing procedures outlined at 42 C.F.R. § 405.1000 through § 405.1054. See 70 Fed. Reg. 11420, 11424-26 (Mar. 8, 2005).

"The issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in a party's favor. (For purposes of this provision, the term "party" does not include a representative of CMS or one of its contractors that may be participating in the hearing.) However, if evidence presented before the hearing causes the ALJ to question a favorable portion of the determination, he or she notifies the parties before the hearing and may consider it an issue at the hearing." 42 C.F.R. § 405.1032(a).

"An ALJ may also issue a decision on the record on his or her own initiative if the evidence in the hearing record supports a fully favorable finding." See 42 C.F.R. §§ 405.1000(g) and (e) and .1038(a). In addition, "[i]f all parties to the hearing waive their right to appear at the hearing in person or by telephone or video-teleconference, the ALJ may make a decision based on the evidence that is in the file and any new evidence that is submitted for consideration." 42 C.F.R. § 405.1000(e).

C. Standard of Review

"The ALJ conducts a de novo review and issues a decision based on the hearing record." (42 C.F.R. § 405.1000(f)).

II. Principles of Law

A. Statutes and Regulations

Part B of Title XVIII of the Social Security Act, the Supplementary Medical Insurance program, provides coverage for a variety of medical services and supplies furnished by physicians, or by others in connection with physicians' services, for outpatient hospital services, and for a number of other specific health-related items and services. Individuals participate voluntarily in the Medicare Part B program and pay a monthly premium.

Section 1862(a)(1) of the Social Security Act excludes Medicare payment for services which "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

Section 1832(a) of the Act states, in pertinent part: The benefits provided to an individual by the insurance program established by this part shall consist of

- (1) entitlement to have payment made to him or on his behalf (subject to the provisions of this part) for medical or other health services...

Pursuant to 42 C.F.R. § 410.20(a) and (b), Medicare Part B pays for physicians' services, including diagnosis, therapy, surgery, consultations, and home, office, and institutional calls, when furnished by qualified professionals.

Section 1833(e) of the Act states that "[n]o payment shall be made to any provider of services or other person under this part unless there has been furnished such information as may be necessary in order to determine the amounts due such provider or other person under this part for the period with respect to which the amounts are being paid or for any prior period." It is expected the patient's medical records will reflect the need for the care provided, and include, but are not limited to, physician's office records, hospital records, and test reports. The Regulations place the burden on the appropriate party – either the provider, supplier, or beneficiary, to furnish "sufficient information" to determine whether payment is due and the amount of payment. 42 C.F.R. § 424.5(a)(6). Without pertinent documentation, there is no objective means of making a "reasonable and necessary" determination as required by § 1862(a)(1)(A) of the Act.

Section 1879(a) of the Act provides that if the services provided are deemed to be not reasonable and necessary for the diagnosis and treatment of an illness or injury or to improve the functioning of a malformed body member or are deemed to be custodial, payment under Part B may still be made if both the Beneficiary and the Provider of the services did not know, nor reasonably should have been expected to know, that the services would not be reimbursable by Medicare. If no payment may be made under this section, the Beneficiary's liability for the charges incurred may be waived if the Beneficiary did not know, nor reasonably should have been expected to know, that the services would not be reimbursable by Medicare. (§ 1879(b)).

B. Policy and Guidance

"The primary authority for all coverage provisions and subsequent policies is the Social Security Act (the Act). Contractors use Medicare policies in the form of regulations, NCDs [*national coverage determinations*], coverage provisions in interpretive manuals, and LCDs [*local coverage determinations*] to apply the provisions of the Act." Medicare Program Integrity Manual (MPIM) (Internet-Only Manual Publ'n 100-08) ch. 13, § 13.1 (May 2004). Section 1871(a)(2) of the Act provides that unless promulgated as a regulation by The Centers for Medicare and Medicaid Services (CMS), no rule, requirement, or statement of policy, other than a National Coverage Determination (NCD), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. § 405.1060. The CMS administers the Medicare Program (Act §§ 1102, 1871, and 1874) and contracts with carriers and intermediaries (Medicare contractors) to act on its behalf in

determining and making payments to providers and suppliers of Medicare items and services. Act §§ 1816 and 1842. In lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical review policies (LMRPs) or local coverage determinations (LCDs). Medicare contractors issue written determinations, called LCDs, specifying under what clinical circumstances a service is considered to be reasonable and necessary. They are administrative and educational tools to assist providers in submitting correct claims for payment. MPIM, *Id.*, § 13.1.3. Contractors publish LCDs to provide guidance to the public and medical community within their jurisdictions whether, on a contractor-wide basis, a particular item or service is covered. Act, § 1869(f)(2)(B). LCDs are used only on a contractor-wide basis and may differ between contractors in different regions of the country.

An ALJ is not bound by LCDs, LMRPs, or CMS program guidance, such as program memoranda and manual instructions, but will give substantial deference to these policies if they are applicable to a particular case. See 42 C.F.R. § 405.1062(a). If an ALJ declines to follow a policy in a particular case, the ALJ decision must explain the reasons why the policy was not followed. See 42 C.F.R. § 405.1062(b).

In the CMS, Medicare National Coverage Determinations Manual (“MNCDM”) (Internet-Only Manual Publ’n 100-03) ch. 1 (May 2005), CMS “describes whether specific medical items, services, treatment procedures, or technologies can be paid for under Medicare. National coverage decisions have been made on the items addressed in this manual. All decisions that items, services, etc. are not covered are based on § 1862(a)(1) of the Act (the “not reasonable and necessary” exclusion) unless otherwise specifically noted.” *Id.*, Part 1, Foreword. National Coverage Determinations (NCDs) made under § 1862(a)(1) of the Act are binding on ALJs during the claim appeal process. See 42 C.F.R. § 405.1060.

For the period of time relevant to this case, the Medicare Contractor, Noridian Healthcare Solutions, issued a medical policy titled LCD for Tumor Treatment Field Therapy (TTFT) (L34823), which indicated that TTFT services were not reasonable and necessary during the date of service at issue.

Analysis

The QIC upheld the denial, finding the documentation did not support the TTFT services (E0766) were reasonable and necessary. The Appellant contends that Medicare coverage and reimbursement is warranted in this case. Careful consideration of the entire record and applicable law supports the ALJ’s determination that the procedure at issue warrants coverage under Medicare Part B.

Initially, the ALJ notes the LCD for Tumor Treatment Field Therapy (TTFT) (L34823), which was controlling during the dates of service at issue, indicates TTFT services are not reasonable and necessary. However, after careful consideration of the evidence included in the record, the ALJ declines to follow the language of the LCD because the evidence supports the procedure was reasonable and necessary for the Beneficiary during the date of service at issue. Significantly, the

Appellant submitted numerous peer reviewed medical studies, statements from physicians and professional societies, and insurance coverage policies, all of which show the procedure was accepted as a safe and effective medical procedure. Moreover, the ALJ is persuaded by the fact that the Beneficiary is benefiting from TTFT. Accordingly, after careful consideration of all the evidence in the record, the ALJ declines to follow the LCD and finds that TTFT services at issue are reasonable and necessary. Accordingly, the ALJ finds the TTF services (E0766) at issue meets Medicare criteria for reimbursement.

CONCLUSIONS OF LAW

The Appellant satisfied the applicable coverage criteria for reimbursement under Part B of the Act for the TTFT services (E0766) that it furnished to the Beneficiary from November 8, 2017, to January 8, 2018. Therefore, as a matter of law, the TTFT services (E0766) furnished on the above date was reasonable and necessary under § 1862(a) of the Act, and the documentation requirements of § 1833(e) were sufficiently satisfied for Medicare to provide reimbursement.

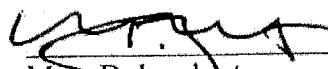
ORDER

For the reasons discussed above the Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Date

11/20/18



Marc D. Lambert

U.S. Administrative Law Judge

3315



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Mid-Atlantic Field Office
Arlington, Virginia

Appeal of:	ALJ Appeal No.: 1-3429199331
Beneficiary:	Medicare Part: Part C
HICN: *****7179A	Before: J. Gerard Lewis U.S. Administrative Law Judge

DECISION

After consideration of the evidence and arguments presented in the record, a **FULLY FAVORABLE** decision is entered for the Appellant.

PROCEDURAL HISTORY

The Appellant submitted a claim for pre-approval of electrical stimulator cancer treatment. The claim was denied initially because the Plan determined that the treatment was not reasonable and necessary. The Appellant appealed and the Plan again denied the claim.

The claim was sent to Maximus Federal Services, and on July 28, 2014, Maximus denied the claim finding that the treatment is not covered by Medicare. The Appellant submitted a timely request for Administrative Law Judge ("ALJ") hearing to the Office of Medicare Hearings and Appeals ("OMHA") on August 6, 2015. A telephone hearing was held in Arlington, Virginia on September 24, 2015.

ISSUES

Whether the Plan, Cigna-Healthspring, is required to pre-approve Novocure Optune Equipment for tumor treatment field therapy?

LEGAL FRAMEWORK

I. Administrative Law Judge Authority, Jurisdiction, Scope of Review and Standard of Review

MB

An individual or organization that is dissatisfied with a reconsideration of a Carrier's initial determination is entitled to a hearing before the Secretary provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Title XVIII § 1869(b)(1)(A) of the Act. The Secretary administers the nationwide hearings and appeals system through the Office of Medicare Hearings and Appeals ("OMHA"). Administrative Law Judges ("ALJs") within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *See* 74 Fed. Reg. 65297 (December 9, 2009).

All initial determinations by the Centers for Medicare and Medicaid Services ("CMS") contracted Intermediaries or Carriers *prior* to January 1, 2006, are governed by the ALJ hearing procedures set forth at 20 C.F.R. §§ 404.929 through 404.961 *and* 42 C.F.R. §§ 405.720 and 405.855. Initial determinations by the CMS contracted Intermediaries or Carriers *after* January 1, 2006, are governed by the ALJ hearing procedures set forth at 42 C.F.R. §§ 405.1000 through 405.1054.

With respect to the dates of service at issue, a request for ALJ hearing meets the amount in controversy requirement if it comports with 42 C.F.R. § 405.1006(b)(1). A request for ALJ hearing is timely if filed within sixty days after receipt of the notice of the Qualified Independent Contractor ("QIC") decision. *See* 42 C.F.R. § 405.1002(a)(1).

OMHA is staffed with ALJs who are qualified and appointed pursuant to the Administrative Procedure Act. They act as independent finders of fact in conducting hearings pursuant to Title XVIII § 1869 of the Act. ALJs conduct 'de novo' hearings of the facts and law. *See* 42 C.F.R. § 405.1000(d); 74 Fed. Reg. 65,316 (Dec. 9, 2009).

Issues before the ALJ include all the issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in Appellant's favor. However, if the evidence presented before or during the hearing causes the ALJ to question a favorable portion of the determination, he or she will notify Appellant and will consider it an issue at the hearing. 42 C.F.R. § 405.1032(a). The ALJ may decide a case on the record and not conduct an oral hearing if the evidence in the hearing record supports a finding in favor of appellants on every issue. 42 C.F.R. § 405.1038(a).

II. Principles of Law, *Part C*

When Congress passed the Balanced Budget Act of 1997 ("BBA"), it added sections 1851 through 1859 to the Act to establish a new Part C of the Medicare program, known as Medicare+Choice ("M+C"). The legislation incorporated private managed care organizations more fully into the Medicare system in order to accommodate delivery of medical services by traditional managed care plans such as Health Maintenance Organizations ("HMOs"), which had experienced problems under the reimbursement model used for Parts A and B, and to offer new plan options for health care. Subsequently, the Medicare Prescription Drug, Improvement and Modernization Act of 2003 ("MMA") renamed the program "Medicare Advantage" and expanded it to allow

for additional private plan structures such as preferred provider organizations ("PPOs") and special needs plans ("SNPs").

Pursuant to Title XVIII § 1852 of the Act, MA Organizations are required to furnish to members the same benefits provided under Original Medicare. Specifically, an MA Organization is required to furnish benefits that would otherwise be covered under Medicare Parts A and B ("Original Medicare") to individuals residing in the area served by the plan.

The Medicare program is set forth in Title XVIII of the Social Security Act ("Act"). Under Title II of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), the Medicare Advantage (MA) program was announced as a replacement to the Medicare + Choice (M+C) managed care program. An MA Plan must provide the services currently available under Medicare Parts A and B, and may provide additional services if specified in its policy. 42 CFR §422.100(a).

Pursuant to 42 CFR §422.101, while enrolled in a MA plan, an enrollee is entitled to and restricted by the limitations and conditions of that program with respect to Medicare coverage and reimbursement. In turn, the MA plan must make available to an enrollee, or provide reimbursement for, at least all services covered under Part A and Part B of Medicare.

III. Principles of Law, Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. *See also* 42 C.F.R. §405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that establishes criteria for coverage of selected types of medical items and services in the form of manuals and local coverage determinations ("LCDs"). Administrative Law Judges are not bound by LCDs, but will give substantial deference to these policies when applicable. 42 C.F.R. §405.1062. If an Administrative Law Judge does not follow a policy in a particular case, the Administrative Law Judge must explain why in the decision. 42 C.F.R. §405.1062.

According to the Local Coverage Determination for Tumor Treatment Field Therapy (TTFT), L34665:

For any item to be covered by Medicare, it must 1) be eligible for a defined Medicare benefit category, 2) be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member, and 3) meet all other applicable Medicare statutory and regulatory requirements. For the items addressed in this local coverage determination, the criteria for "reasonable and necessary", based on Social Security Act § 1862(a)(1)(A) provisions, are defined by the following indications and limitations of coverage and/or medical necessity.

For an item to be covered by Medicare, a detailed written order (DWO) must be received by the supplier before a claim is submitted. If the supplier bills for an item addressed in this policy without first receiving the completed DWO, the item will be denied as not reasonable and necessary.

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

FINDINGS OF FACT AND ANALYSIS

The primary issue on appeal is whether the Plan is required to pre-approve tumor treatment field therapy (TTFT) for the Beneficiary. Maximus determined that the Plan was not required to pre-approve the TTFT device finding that the requested treatment is not medically necessary under Medicare. The Appellant contends TTFT is FDA-approved, and would be safe and effective for the Beneficiary.

Pursuant to Medicare rules, a Medicare Advantage plan must provide its enrollees with coverage for all services covered by Medicare. 42 CFR §422.101. The Plan's Evidence of Coverage states that the Plan covers items and services in accordance with Medicare rules. The LCD at issue, L34665, states that TTFT will be denied as not reasonable and necessary.

The LCD should not be followed in this instance because there is sufficient evidence in the medical record to find that the treatment was medically reasonable and necessary. The Beneficiary has received chemotherapy services; however, the record shows that chemotherapy makes the Beneficiary's white blood count drop so low that he must be hospitalized. In addition, he has loss of appetite, dizziness, fatigue, nausea, and brain swelling.

The record shows that TTFT therapy is safe and effective and not experimental or investigational. Also, the treatment has been approved by the FDA. There are numerous clinical studies demonstrating the safety and effectiveness of the treatment. Moreover, the treatment was appropriate for this Beneficiary given his medical history, including low tolerance for alternative treatment. It was reasonable for the physician to prescribe and initiate this treatment as it was the best FDA-approved option at this time for this Beneficiary.

Based on the foregoing, there is sufficient evidence to find that the treatment was reasonable and necessary for this Beneficiary, and it should be approved.

CONCLUSIONS OF LAW

Cigna-Healthspring is required to pre-approve Novocure Optune Equipment for the enrollee for tumor treatment field therapy.

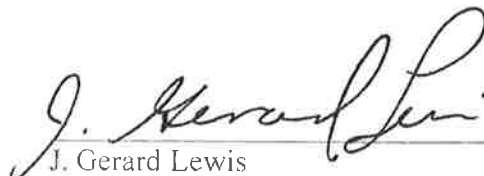
ORDER

The Medicare Contractor is hereby **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

MAY 03 2016

Date


J. Gerard Lewis
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Arlington Field Office
Arlington, Virginia

Appellant:	ALJ Appeal No.:
Beneficiary	Medicare Part: C
HICN: ***** 8864A	Before: J. Gerard Lewis U.S. Administrative Law Judge

DECISION

After carefully considering the evidence and arguments provided in the record, a **FULLY FAVORABLE** decision is entered for: "Appellant").

PROCEDURAL HISTORY

Appellant, was enrolled in Health Alliance Connect, Inc., (PPO) Medicare health advantage plan ("Plan"). The Appellant requested the Plan to pre-approve Tumor Treatment Fields ("TTFields") therapy using Optune Plus Transducers. The Plan initially denied the request. In a request for an expedited appeal, the Plan affirmed denial of coverage. The Appellant requested reconsideration from Maximus Federal Services, the Part C Independent Review Entity ("IRE"). On December 16, 2015, the IRE indicated that the Plan contract covers services in accordance with Medicare rules, found Medicare does not cover TTFields therapy, and reasoned that the Plan was not required to pre-approve TTField therapy. (Exh. 1, pp. 2-4).

On December 23, 2015, the Appellant filed a timely request for hearing by an Administrative Law Judge ("ALJ") at the Office of Medicare Hearings and Appeals ("OMHA"). (Exh. 2, p. 4). The amount in controversy meets the jurisdictional requirements for an ALJ hearing. The hearing was held via telephone conference on February 18, 2016, before Judge J. Gerard Lewis. The Appellant was represented, sworn, and provided testimony. The Appellant's provider, Dan McCoy, case manager at Novocure, Inc., was sworn and provided testimony. The Plan was given notice to participate in the hearing, but did not participate during the hearing. Exhibits 1-5 were admitted into the record without objections. (Hearing CD).

ISSUES

1. Whether the Plan is required to pre-approve TTFields therapy pursuant to the statutory and regulatory provisions under Part C of Title XVIII of the Social Security Act, 42 C.F.R. § 422. *et seq.*, and the Plan's Evidence of Coverage.

FINDINGS OF FACT

1. The Appellant requested pre-approval for TTFields therapy (E0766) using Optune Plus Transducers.
2. Appellant was diagnosed with glioblastoma mutiforme ("GBM") in June 2015 and underwent a craniotomy for resection of his tumor. (Exh. 1, p. 81). (Exh. 4, p. 1).
3. On September 17, 2015, the Appellant completed radiation therapy with concurrent temozolomide. (Exh. 1, p. 83). (Exh. 4, p. 1).
4. In October 2015, the Federal Drug Administration ("FDA") granted Optune pre-market approval for newly diagnosed glioblastoma in combination with temozolomide after standard surgical resection and radiation therapy. (Exh. 4, p. 2).
5. On October 16, 2015, the physician prescribed Optune therapy and the Beneficiary began Optune treatment in combination with temozolomide that month. (Exh. 1, pp. 69, 82, 85). (Exh. 4, p. 1).
6. Optune is a portable battery, or power supply, delivering TTFields to the brain of individuals with newly diagnosed or recurrent GBM. (Exh. 4, p. 23).
7. On December 15, 2015, the Journal of American Medical Association ("JAMA") published evidence from a definitive randomized clinical trial indicating that patients with glioblastoma who completed standard chemoraditiaeon therapy had a significantly prolonged progression-free and overall survival when the TTFields were added to temozolomide chemotherapy. (Exh. 5, pp. 1-9).
8. MRI results indicate that the Beneficiary's brain tumor remained in a stable condition given its lack of growth after being treated with Optune in combination with temozolomide. (Hearing CD).

LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

An individual or organization that is dissatisfied with a reconsideration of a Contractor's initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services ("Secretary") provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. Social Security Act § 1869(b)(1)(A). The Secretary administers the nationwide hearings and appeals system through the Office of Medicare Hearings and Appeals ("OMHA"). Administrative Law Judges ("ALJs") within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. *See* 74 Fed. Reg. 65297 (December 9, 2009).

A request for hearing meets the amount in controversy requirement if it comports with 42 C.F.R. § 405.1006(b)(1). A request for hearing is timely if filed within sixty days after receipt of the notice of the Qualified Independent Contractor decision. 42 C.F.R. § 405.1002(a)(1).

B. Scope of Review

"The issues before the administrative law judge include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in [the appellant's] favor. However, if evidence presented before or during the hearing causes the administrative law judge to question a fully favorable determination, he or she will notify [the appellant] and will consider it an issue at the hearing." 42 C.F.R. § 405.1032(a).

The ALJ may decide a case on the record and not conduct an oral hearing if the decision is fully favorable, or if the appellant indicates in writing that he does not wish to appear before the ALJ at a hearing. 42 C.F.R. § 405.1038.

C. Standard of Review

"The ALJ conducts a de novo review and issues a decision based on the hearing record." 42 C.F.R. § 405.1000(d).

II. Principles of Law

A. Statutes and Regulations

According to § 1862(a)(1)(A) of the Social Security Act ("Act"), Medicare may not make a payment under part A or part B for anything which is not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Section 1862(a)(12) states:

(a) Notwithstanding any other provision of this title, no payment may be made under part A or part B for any expenses incurred for items or services —

(12) where such expenses are for services in connection with the care, treatment, filling, removal, or replacement of teeth or structures directly supporting teeth, except that payment may be made under part A in the case of inpatient hospital services in connection with the provision of such dental services if the individual, because of his underlying medical condition and clinical status or because of the severity of the dental procedure, requires hospitalization in connection with the provision of such services;

Section 1852(a) of the Act outlines the basic benefits in a case involving a Medicare Advantage (“MA”) Organization and states in pertinent part:

(1) (A) In general.—Except as provided in section 1859(b)(3) for MSA plans and except as provided in paragraph (6) for MA regional plans, each Medicare+Choice plan shall provide to members enrolled under this part, through providers and other persons that meet the applicable requirements of this title and part A of title XI, benefits under the original Medicare fee-for-service program option (and, for plan years before 2006, additional benefits required under section 1854(f)(1)(A))

(B) Benefits under the original Medicare fee-for-service program option defined.—

(i) In general.—For purposes of this part, the term “benefits under the original Medicare fee-for-service program option” means those items and services (other than hospice care) for which benefits are available under parts A and B to individuals entitled to benefits under part A and enrolled under part B, with cost-sharing for those services as required under parts A and B or, subject to clause (iii), [418] an actuarially equivalent level cost-sharing as determined in this part.

The general regulations for Medicare Advantage Organizations are outlined in 42 C.F.R. § 422.100 which states “An MA organization must make timely and reasonable payment to or on behalf of the plan enrollee for the following services obtained from a provider or supplier that does not contract with the MA organization to provide services covered by the MA plan.”

The requirements relating to basic benefits are outlined in 42 C.F.R. § 422.101 and state:

Except as specified in Sec. 422.318 (for entitlement that begins or ends during a hospital stay) and Sec. 422.320 (with respect to hospice care), each MA organization must meet the following requirements:

(a) Provide coverage of, by furnishing, arranging for, or making payment for, all services that are covered by Part A and Part B of Medicare (if the enrollee is entitled to benefits under both parts) or by Medicare Part B (if entitled only under Part B) and that are available to beneficiaries residing in the plan's service area. Services may be provided outside of the service area of the plan if the services are accessible and available to enrollees.

(b) Comply with--

(1) CMS's national coverage determinations; (2) General coverage guidelines included in original Medicare manuals and instructions unless superseded by regulations in this part or referred instructions; and (3) Written coverage decisions of local Medicare contractors with jurisdiction for claims in the geographic area in which services are covered under the MA plan.

The guidelines for access to services for Medicare Advantage plan member are set out in 42 C.F.R. § 422.112 and states "An MA organization that offers an MA coordinated care plan may specify the networks of providers from whom enrollees may obtain services if the MA organization ensures that all covered services, including supplemental services contracted for by (or on behalf of) the Medicare enrollee, are available and accessible under the plan."

An MA organization is required to comply with CMS national coverage determinations, general coverage guidelines included in original Medicare manuals and instructions and the written coverage decisions of local Medicare contractors with jurisdiction for claims in the geographic area in which the services are covered under the MA plan. 42 C.F.R. § 422.101(b).

Under 42 C.F.R. § 422.111, the Plan must disclose to its enrollees in clear, accurate terms all the benefits offered under a Plan, including applicable conditions and limitations, premiums and cost-sharing (such as copayments, deductibles, and coinsurance) and any other conditions associated with receipt or use of benefits.

Particular services are excluded from coverage including examinations performed for a purpose other than treatment or diagnosis of a specific illness, symptoms, complaint, or injury, except for screening mammography, colorectal cancer screening tests, screening pelvic exams, prostate cancer screening tests, glaucoma screening exams, ultrasound screening for abdominal aortic aneurysms (AAA), cardiovascular disease screening tests, diabetes screening tests, a screening electrocardiogram. 42 C.F.R. § 411.15.

B. National Coverage Determination

A National Coverage Determination ("NCD"), if applicable, is binding on the ALJ. 42 C.F.R. §405.1060(a)(4). The applicable NCD in this case is § 280.14 and can be found at CMS, Medicare National Coverage Determinations Manual ("MNCDM"), 100-3, ch. 1, § 280.14.

C. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by Centers for Medicare and Medicaid Services ("CMS"), no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. See also 42 C.F.R. §405.860. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that establishes criteria for coverage of selected types of

medical items and services in the form of manuals and local coverage determinations (“LCDs”). Administrative Law Judges are not bound by LCDs, but will give substantial deference to these policies when applicable. 42 C.F.R. §405.1062. If an Administrative Law Judge does not follow a policy in a particular case, the Administrative Law Judge must explain why in the decision. 42 C.F.R. §405.1062.

CMS issued the *Medicare Managed Care Manual (“MMCM”) (Internet-Only Manual Publ’n 100-16)*, ch. 10, (August 2011), sets forth specific guidance regarding Medicare Advantages plans.

LCD L34823, states in pertinent part:

Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary.

Article Policy **A52711** expressly states: Tumor treatment field therapy devices are covered under the Durable Medical Equipment benefit (Social Security Act § 1861(s)(6)). In order for a beneficiary’s equipment to be eligible for reimbursement the reasonable and necessary (R&N) requirements set out in the related Local Coverage Determination must be met. Code E0766 is in the frequent and substantial service payment category. Items included in this payment category are reimbursed a single monthly fee schedule amount for the device and all related supplies and accessories.

When a NCD or LCD or other directives are lacking, the adjudication process requires the Judge to determine coverage by performing the same review that Medicare contractors, according to the Medicare Program Integrity Manual (Publ. 100-08), Chapter 13.7.1, would perform when developing a LCD.

Contractor LCDs shall be based on the strongest evidence available. The extent and quality of supporting evidence is key to defending challenges to LCDs. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on:

- Published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and
- General acceptance by the medical community (standard of practice), as supported by sound medical evidence based on:
- Scientific data or research studies published in peer-reviewed medical journals;
- Consensus of expert medical opinion (i.e., recognized authorities in the field: or
- Medical opinion derived from consultations with medical

associations or other health care experts.

D. Evidence of Coverage

The Plan's Evidence of Coverage states our Medicare covered services must be provided according to the coverage guidelines established by Medicare. (Exh. 1, pp. 2-4).

ANALYSIS

The Appellant is seeking pre-approve for TTFields therapy (E0766) using Optune Plus Transducers. On December 16, 2015, the IRE indicated that the Plan contract covers services in accordance with Medicare rules, found Medicare does not cover TTFields therapy, and reasoned that the Plan was not required to pre-approve TTField therapy. (Exh. 1, pp. 2-4).

Pursuant to 42 C.F.R. § 422.101, a Medicare Advantage organization must (1) provide coverage all services that are covered by Part A or Part B of Medicare, and (2) comply with all national coverage determinations, coverage guidelines in original Medicare manuals and instructions, and the written coverage decisions of local Medicare contractors with jurisdiction. The Plan's Evidence of Coverage states the Plan covers items and services in accordance with Medicare rules.

In this instance, the applicable LCD L34823 states that Tumor treatment field therapy (E0766) will be denied as not reasonable and necessary. While the undersigned gives substantial deference to this LCD provision, the record contains published authoritative evidence derived from a definitive randomized clinical trial and scientific data published in a peer-reviewed medical journal indicating that TTFields therapy is reasonable and necessary for individuals newly diagnosed with glioblastoma. On December 15, 2015, the Journal of American Medical Association ("JAMA"), a peer-reviewed medical journal, published an article entitled "Maintenance Therapy with Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma a Randomized Clinical Trial." (Exh. 5, pp. 1-9). The clinical trial included 695 patients. (*Id.* at 4). Patients eligible to participate in the clinical trial were (1) diagnosed with glioblastoma, (2) progression-free after having safe debulking surgery or biopsy, and (3) completed standard concomitant chemoradiotherapy with temozolomide. (*Id.* at 2). The patients were randomized to receive TTFields with temozolomide (466 patients) or temozolomide alone (229 patients). (*Id.* at 4). Notably, the trial was pre-approved by the FDA and trial recruitment closed on November 29, 2014. (*Id.*). The results of the trial concluded that "adding TTFields and temozolomide chemotherapy significantly prolonged progression-free and overall survival." (*Id.* at 8). Specifically, "patients randomized to receive TTFields plus temozolomide compared with patients randomized to receive temozolomide alone had a median progression-free survival of 7.1 months vs 4.0 months. Patients who received TTFields plus temozolomide had a median overall survival of 20.5 months compared with 15.6 months of those who received temozolomide alone." (*Id.* at 7). Additionally, "the percentage of patients alive at 2 years following enrollment was 43% in the TTFields plus temozolomide group and was 29% in the temozolomide alone group." (*Id.* at 6). Consequently, the trial's independent data and safety

monitoring committee recommend early termination of the trial and patients in the temozolomide alone group were allowed to cross over to the TTFields plus temozolomide group. (*Id.*). (Hearing CD). The results of these studies prompted the FDA to grant Optune pre-market approval in October 2015 for newly diagnosed glioblastoma in combination with temozolomide after standard surgical resection and radiation therapy. (Exh., 4, p. 2). (Hearing CD). Therefore, the results of this study and subsequent FDA pre-market approval indicate that TTFields therapy is a reasonable and necessary treatment for individuals with glioblastoma who are also receiving temozolomide.

In the present case, the Appellant meets the participant criteria outlined in the JAMA article and FDA pre-market approval. The Appellant's was newly diagnosed with glioblastoma, underwent a craniotomy for resection of his tumor, and completed radiation therapy with concurrent temozolomide. (Exh. 4, p. 1). (Exh.1, pp. 81, 83). Consequently, the Appellant's physician prescribed Optune in combination with temozolomide as the ideal treatment plan for the Beneficiary's condition. (Exh. 1, p. 69). The Beneficiary began treatment in October 2015 during the same month and year that Optune received pre-market approval for this treatment. (Exh. 1, p. 69). (Exh. 4, p. 2). (Hearing CD). Because glioblastoma is a very aggressive disease, the Beneficiary decided to proceed with the treatment even though his pre-approval request was denied. (Hearing CD). Notably, the Appellant's quality of life has improved. He has remained in a stable condition since beginning the treatment and an MRI indicates no tumor growth. (*Id.*). The Appellant's provider explained that the company's directory of health policy has met with CMS several times; however, the issue is that the scientific data relevant to the Appellant's case is relatively new given that Optune received FDA pre-market approval in October 2015 and the JAMA article was published in December 2015. (*Id.*). (Exh. 4, p. 2). (Exh. 5, pp. 1-9). (Hearing CD). Nevertheless, the Appellant's improved quality of life after use of Optune concurrent with temozolomide supports the JAMA article findings that TTField therapy is a reasonable and necessary treatment for individuals with newly diagnosed glioblastoma. Accordingly, the Plan is required to pre-approve the tumor treatment field therapy pursuant to § 1852 of the Act.

CONCLUSIONS OF LAW

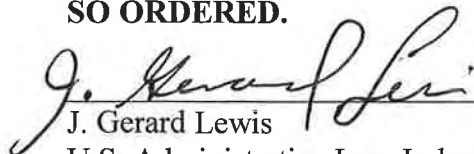
The Plan is required to pre-approve TTFields therapy (E0766) using Optune Plus Transducers pursuant to the statutory and regulatory provisions under Part C of Title XVIII of the Social Security Act, 42 C.F.R. § 422. *et seq.*, and the Plan's Evidence of Coverage.

ORDER

The Medicare Contractor is hereby **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: MAY 10 2016


J. Gerard Lewis
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Arlington Field Office
Arlington, Virginia

Appeal of:	ALJ Appeal No.: 1-7866860304
Beneficiary:	Medicare: Part B
HICN:	Before: J. Gerard Lewis Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record and at the hearing, a **FULLY FAVORABLE** decision is entered for (“the Appellant/Beneficiary”).

PROCEDURAL HISTORY

Novocure, Inc. (“Provider”) submitted a claim for reimbursement of rental of an electronic stimulation cancer treatment (Optune) device (E0766) provided to the Appellant from October 27, 2017 to January 27, 2018. CGS Administrators, LLC, the Medicare Administrative Contractor (“Contractor”) denied payment initially and upon redetermination. The Appellant requested reconsideration from the Qualified Independent Contractor (“QIC”). On August 16, 2018, the QIC upheld the denial stating that tumor treatment field therapy (CPT E0766) was denied as not reasonable and necessary under the applicable Local Coverage Determination (“LCD”), and that there was insufficient documentation to quantify the effects of the device. The QIC found the Provider liable for non-covered charges. (Exh. 1, pp. 1-7).

On September 10, 2018, the Office of Medicare Hearings and Appeals (“OMHA”) received the Appellant’s timely filed request for a hearing before an Administrative Law Judge (“ALJ”). (Exh. 3, pp. 1-2). The amount in controversy meets the jurisdictional requirements for an ALJ appeal decision. 42 C.F.R. §405.1006.

A hearing was held via telephone conference on October 17, 2018, before Judge J. Gerard Lewis. Ms. Debra Parrish, Esq. appeared on behalf of the Appellant and provided argument. Exhibits 1-4 were admitted without objections. (Hearing CD). The administrative record is now closed.

ISSUES

1. Whether the electronic stimulation cancer treatment (Optune) device (E0766) provided to the Appellant from October 27, 2017 to January 27, 2018 meets Medicare coverage criteria.
2. Whether the services provided are medically necessary under §1862(a)(1)(A) of the Social Security Act ("the Act") and reimbursable under Medicare.
3. If the services are found to be excluded from coverage under §1862(a)(1)(A) of the Act, whether payment may nevertheless be made to the Appellant under the limitation on liability provisions of §1879 of the Act.

FINDINGS OF FACT

1. The Appellant was a 64-year-old male who was newly diagnosed with glioblastoma multiforme ("GBM") on August 6, 2017, and underwent a left temporoparietal craniotomy and tumor resection on August 9, 2018. (Exh. 2, p. 16).
2. Post-surgical imaging of the Appellant's brain indicated peripherally enhancing mass internal susceptibility artifact that may represent blood products and seen surrounding edema. A peripherally enhancing mass that demonstrated restricted diffusion could also be seen in the setting of an abscess. (Exh. 2, pp. 19-20).
3. The Appellant received a neuro-oncology evaluation for a second opinion after meeting with a radiation oncologist and a medical oncologist. The Beneficiary was noted to have speech difficulty, confusion, and decreased concentration. The physician's impression was that the Appellant had GBM, NOS, and referred the Appellant to an additional specialist. (Exh. 2, pp. 1-4).
4. On August 23, 2017, the Appellant's physician prescribed use of an Optune device for a period of six months, with a preferred treatment start date of September 1, 2017. (Exh. 1, p. 23).
5. The Beneficiary received TTFT from at least October 27, 2017 through January, 27, 2018. (Exh. 1, pp. 42-45).
6. The record includes a letter dated August 7, 2018 from CGS Administrators, LLC to the Provider in response to a reconsideration request for TTFT LCD 34823. The letter states that the TTFT LCD includes language indicating that the coverage of TTFT for recurrent GBM is not reasonable and necessary, but that coverage of newly diagnosed GBM is not addressed. The letter reflects the Provider submitted a valid request to add coverage for newly diagnosed GBM, but the request to add coverage for recurrent GBM was invalid. Additionally, the letter states that the Provider would receive a decision on the request by September 18, 2018. (Exh. 4).

LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction, Scope of Review, and Standard of Review

An individual who is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before an ALJ provided there is a sufficient amount in controversy and the individual timely requests a hearing. Act §§205(b), 1869(b)(1)(A), (d)(1); *see also* 42 C.F.R. §§405.924(b), 405.1000(a), 405.1002(a), 405.1014.

The issues before an ALJ include all issues brought out in the initial determination, redetermination, or reconsideration that were not decided entirely in an appellant's favor. 42 C.F.R. §405.1032(a). An ALJ conducts a *de novo* review and issues a decision based on the administrative record, including the hearing record. 42 C.F.R. §405.1000(d).

Appellant has the burden of proving each element of a Medicare claim by a preponderance of the evidence. *See* Act §1833(e); 42 C.F.R. §§405.1018, 405.1028, 405.1030, and 424.5(a)(6).

II. Principles of Law

A. Statutes and Regulations

Section 1831 establishes the Supplemental Medical Insurance Program for the aged and disabled under Medicare Part B. Section 1832 establishes the scope of benefits that are provided to beneficiaries under the Medicare Part B insurance program. Under §1832(a)(2)(B), an individual is entitled to have payment made on his/her behalf for medical and other health services furnished by a provider of services or by others under arrangement with them made by a provider of services. *See also* 42 C.F.R. §410.3. Section 1833(e) provides that "[n]o payment shall be made to any provider of services... unless there has been furnished such information as may be necessary in order to determine the amounts due such provider..." *See also* 42 C.F.R. §424.5(a)(6).

Section 1861(n) defines the term "durable medical equipment." *See also* 42 CFR §410.38. Section 1861(s)(6) defines the term "medical and other health services" and specifically includes durable medical equipment. *See also* 42 C.F.R. §410.10(h), 42 C.F.R. §§414.200-232 implements §1834 (a) and (h) of the Act by specifying how payments are made for the purchase or rental of new and used durable medical equipment and prosthetic and orthotic devices for Medicare beneficiaries. Section 1862(a)(1)(A) provides that notwithstanding any other provision of the Act, no payment shall be made for any expenses incurred for items and services that are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. *See also* 42 C.F.R. §411.15(k).

Section 1879 limits liability when items or services are not covered because they are found to be not medically reasonable or necessary under §1862(a)(1) (or in a few other limited circumstances). Limitation is based upon a party's lack of knowledge of non-coverage. *See also* 42 C.F.R. §§411.400 to 411.408; CMS, *Medicare Claims Processing Manual (MCPM) (Internet-Only Manual Publ'n 100-4)* ch. 30, (May 2007).

B. National Coverage Determinations

A National Coverage Determination ("NCD"), if applicable, is binding on the ALJ. 42 C.F.R. §405.1060(a)(4). There is no applicable NCD in this case.

C. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement or statement of policy, other than a National Coverage Determination ("NCD"), can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued policy guidance that describe criteria for coverage of selected types of medical items and services in the form of manuals and local medical-review policies ("LMRPs") or local coverage determinations ("LCDs"). CGS Admins., LLC, Local Coverage Determination L34823: Tumor Treatment Field Therapy ("TTFT") (LCD L34823) is applicable to this appeal.

ANALYSIS

The issue is whether the electronic stimulation cancer treatment (Optune) device (E0766) provided to the Appellant from October 27, 2017 to January 27, 2018 meets Medicare coverage criteria. QIC denied payment stating that tumor treatment field therapy (E0766) was not reasonable and necessary under the applicable Local Coverage Determination ("LCD"), and that there was insufficient documentation to quantify the effects of the device. The QIC found the Provider liable for non-covered charges. (Exh. 1, pp. 1-7).

Here, LCD L34823 does not apply. The LCD states that TTFT will be denied as not medically reasonable and necessary. However, a letter from the Contractor, dated August 7, 2018 states that "[c]urrently, the TTFT LCD includes language that the coverage of TTFT for recurrent glioblastoma multiforme (GBM) is not reasonable and necessary. Coverage of newly diagnosed GBM is not addressed." (Exh. 4). Additionally, the Contractor stated the Provider submitted a valid request to reconsider the LCD to add coverage for TTFT for newly diagnosed GBM, and the Contractor is currently considering that request. (*Id.*).

The Appellant was a 64-year-old male who was newly diagnosed with GBM on August 6, 2017, and underwent a left temporoparietal craniotomy and tumor resection on August 9, 2018. (Exh. 2, p. 16). Post-surgical imaging of the Appellant's brain indicated peripherally enhancing mass internal susceptibility artifact that may represent blood products and seen surrounding edema. A peripherally enhancing mass that demonstrated restricted diffusion could also be seen in the setting of an abscess. (*Id.* at 19-20). On August 23, 2017, the Appellant's physician prescribed use of an Optune device for a period of six months, with a preferred treatment start date of September 1, 2017. (Exh. 1, p. 23). The Appellant received TTFT from at least October 27, 2017 through January, 27, 2018. (Exh. 1, pp. 42-45). At the hearing, Ms. Parrish stated that the Appellant's initial prognosis was 10 months, but that he responded well to TTFT, and was continuing to use, and benefit from the treatment. (Hearing CD). The Appellant in this case was newly diagnosed with GBM, and based on the Contractor's own language, the LCD does not apply. Additionally, the evidence and testimony indicates that TTFT was medically reasonable and necessary because the Appellant continues to use and benefit from the treatment.

Moreover, Ms. Parrish reiterated that the FDA's clinical trials for TTFT were concluded early because the treatment showed significant effectiveness. The record shows that TTFT therapy is safe and effective and not experimental or investigational. There are numerous clinical studies demonstrating the safety and effectiveness of the treatment. Based on the Appellant's new diagnosis and medical condition it was reasonable for his physician to prescribe and initiate this treatment as the best FDA-approved option.

Based on the foregoing considerations, there is sufficient evidence to find that the treatment was reasonable and necessary for this Appellant, and meets Medicare's coverage requirements.

CONCLUSIONS OF LAW

The electronic stimulation cancer treatment (Optune) device (E0766) provided to the Appellant from October 27, 2017 to January 27, 2018 meets Medicare coverage requirements. The items are medically necessary under Part B of Title XVIII and §1862(a)(1) of the Act.

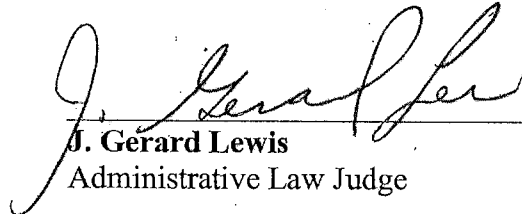
ORDER

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

NOV 07 2018

Dated: _____



J. Gerard Lewis
Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Arlington, Virginia

Appeal of:	OMHA Appeal No.: 1-7905022859
Beneficiary:	Medicare: Part B
Medicare No.:	Before: J. Gerard Lewis Administrative Law Judge

DECISION

After carefully considering the evidence and arguments presented in the record and at the hearing, a **FULLY FAVORABLE** decision is entered for (“Beneficiary”).

PROCEDURAL HISTORY

The Beneficiary submitted a claim to the Medicare Administrative Contractor (“Contractor”) for electric stimulation cancer treatment (E0766), provided to the Beneficiary on September 2, 2017 and February 2, 2018.

The Contractor initially denied payment for the services. Upon redetermination the Contractor again, denied payment. (Exh. 1, pp. 15-16). The Appellant requested reconsideration from the Qualified Independent Contractor (“QIC”). On August 16, 2018, the QIC denied payment stating the records do not support the device is reasonable and necessary, which is required as outlined in the LCD L34823. The QIC found Novocure Inc. responsible for the non-covered services (*Id.* at 1-6).

The Beneficiary, represented by Debra Parrish, JD of Parrish Law Offices, filed a request for an Administrative Law Judge (“ALJ”) hearing at the Office of Medicare Hearings and Appeals (“OMHA”) on October 8, 2018. (Exh. 3, pp. 1-7). The amount in controversy met the jurisdictional requirements for an ALJ hearing.

Judge J. Gerard Lewis held a telephone hearing on October 31, 2018. The Beneficiary was represented by Debra Parrish, JD. The Beneficiary’s representative provided sworn testimony and Exhibits 1-4 were admitted without objection. (Hearing CD). The administrative record is now closed.

ISSUES

1. Whether electric stimulation cancer treatment (E0766), provided to the Beneficiary on September 2, 2017 and February 2, 2018, meet Medicare coverage criteria.
2. Whether the services were medically necessary in accordance with section 1862(a)(1)(A) of the Social Security Act ("Act").
3. If the services are found to be excluded from coverage under section 1862(a)(1)(A) of the Act, whether payment may nevertheless be made to the Appellant under the limitation on liability provisions of section 1879 of the Act.

FINDINGS OF FACT

1. The Appellant is seeking reimbursement for electric stimulation cancer treatment (E0766), provided to the Beneficiary on September 2, 2017 and February 2, 2018.
2. The Beneficiary was a 74 year old woman who was diagnosed with glioblastoma. (Exh. 2, p. 5).
3. On April 9, 2017, the Beneficiary presented to an outside hospital with several weeks of progressive right-sided weakness. A MRI of the brain demonstrated two discrete nodular enhancing lesions-one in the left thalamus and the second in the capsule. The Beneficiary's case was reviewed at brains mets tumor board attended by representatives from the departments of radiation oncology, neuro oncology, and neurosurgery. Closer attention to the MRI revealed T2/FLAIR findings in the left insular cortex, left thalamus, left hippocampus/parahippocampal gyrus and left posterior temporal lobe in addition to the enhancing lesions in thalamus/capsule-very concerning for gliomatosis. Pathology revealed a WHO Grade IV glioblastoma. (Exh. 2, pp. 1- 2).
4. The Beneficiary was seen by her physician on May 2, 2017 and May 15, 2017 for a follow up regarding her newly diagnosed WHO Grade IV glioblastoma. She completed 4 out of a planned 30 doses of radiation and presented to her physician because she was struggling with weakness and constipation. The optune device was discussed but pending insurance. (Exh. 2, pp. 1-11).
5. The record contained two optune prescription forms signed and dated by the Beneficiary's physician on May 2, 2017 and October 18, 2017. The Beneficiary's diagnosis was glioblastoma. The physician prescribed optune which is comprised of an electric field generator, transducer arrays, power supply items, and accessories for 6 months. Preferred treatment start date was ASAP. (Exh. 2, pp. 16-17).

LEGAL FRAMEWORK

I. ALJ Review Authority

A. Jurisdiction

An individual who, or an organization that, is dissatisfied with the reconsideration of an initial determination is entitled to a hearing before the Secretary of the Department of Health and Human Services (“HHS”), provided there is a sufficient amount in controversy and a request for hearing is filed in a timely manner. (Act §1869(b)(1)(A)).

ALJs within OMHA issue the final decisions of the Secretary, except for decisions reviewed by the Medicare Appeals Council. (42 C.F.R. § 405.1100).

A hearing before an ALJ is available only if the remaining amount in controversy is at least \$140.00 for appeals filed on or after January 1, 2014. (42 C.F.R. § 405.1006). The request for hearing is timely filed if filed within 60 days after receipt of a QIC decision. (42 C.F.R. § 405.1002(a)(1)).

B. Scope of Review

“The issues before the administrative law judge include all the issues brought out in the initial, reconsidered or revised determination that were not decided entirely in [the appellant’s] favor. However, if evidence presented before or during the hearing causes the administrative law judge to question a fully favorable determination, he or she will notify [the appellant] and will consider it an issue at the hearing.” 42 C.F.R. § 405.1032(a).

The ALJ may decide a case on the record and not conduct an oral hearing if the decision is fully favorable, or if the appellant indicates in writing that he does not wish to appear before the ALJ at a hearing. When a hearing is not held, the decision of the ALJ must refer to the evidence in the record on which the decision was based. (42 C.F.R. § 405.1038).

C. Standard of Review

“The ALJ conducts a *de novo* review and issues a decision based on the hearing record.” (42 C.F.R. § 405.1000(d)).

II. Principles of Law

A. Statutes and Regulations

The Medicare program, Title XVIII of the Act, is administered through the Centers for Medicare and Medicaid Services (“CMS”), a component of HHS. Under the authority of § 1842(a)(1)(A) of the Act, the Secretary is authorized to enter into contracts with private entities for the day-to-day operations of the program.

Part B of Title XVIII, the Supplementary Medical Insurance program, provides coverage for a variety of medical services and supplies furnished by physicians, or by others in connection with

physicians' services, for outpatient hospital services, and for a number of other specific health-related items and services. Individuals participate voluntarily in the Medicare Part B program and pay a monthly premium. Section 1861(s)(2)(A) of the Act defines the term "medical and other health services" and specifically includes services and supplies furnished as an incident to a physician's professional service. (*See also* 42 CFR § 410.10(b)).

Section 1833(e) of the Act states that "[n]o payment shall be made to any provider of services or other person under this part unless there has been furnished such information as may be necessary in order to determine the amounts due such provider or other person under this part for the period with respect to which the amounts are being paid or for any prior period."

Coverage of medical and other health services is qualified by the overarching principles of the Act, section 1862(a), which provides that Medicare payments will only be made for items or services that are "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member," notwithstanding any other provision of Title XVIII of the Act. (*See also* 42 C.F.R. § 411.15(k)(1)).

If it is determined that Medicare cannot pay for the services at issue, section 1879 of the Act may assign liability for the payment of these services. If the beneficiary had no knowledge that the services would not be covered, but the provider of the services did, then the provider is liable and cannot seek or retain payment by the beneficiary. The regulations at 42 C.F.R. § 411.400 *et seq.* and HCFA Ruling 95-1 address how to determine if the beneficiary or provider/supplier had the requisite degree of knowledge to make them liable under section 1879 of the Act. In general, the existence of a notice, manual, or community medical standard is sufficient to constitute notice as applicable to the provider. (*See also*, 42 C.F.R. § 411.406).

B. National Coverage Determination

A National Coverage Determination ("NCD"), if applicable, is binding on the ALJ. 42 C.F.R. § 405.1060(a)(4). There is no applicable NCD in this case.

C. Policy and Guidance

Section 1871(a)(2) of the Act states that unless promulgated as a regulation by CMS, no rule, requirement, or statement of policy, other than an NCD, can establish or change a substantive legal standard governing the scope of benefits or payment for services under the Medicare program. (*See* 42 C.F.R. § 405.860). However, in lieu of binding regulations with the full force and effect of law, CMS and its contractors have issued manuals and local coverage determinations ("LCDs") as policy guidance and to establish criteria for coverage of selected types of medical items and services. ALJ's are not bound by the manuals or the LCD's, but they are to give substantial deference to these policies when applicable. (42 C.F.R. § 405.1062). If an ALJ does not follow a policy in a particular case, the ALJ must explain why the policy was not followed. (*Id.*).

ANALYSIS

The Appellant is seeking reimbursement for electric stimulation cancer treatment (E0766), provided to the Beneficiary on September 2, 2017 and February 2, 2018.

The Beneficiary was a 74 year old woman who was diagnosed with glioblastoma in April 2017 (Exh. 2, p. 5). The Beneficiary was seen by her physician on May 2, 2017 and May 15, 2017 for a follow up regarding her *newly diagnosed* WHO Grade IV glioblastoma. She completed 4 out of a planned 30 doses of radiation and presented to her physician because she was struggling with weakness and constipation. (*Id.* at 1-11). The record contained two optune prescription forms signed and dated by the Beneficiary's physician on May 2, 2017 and October 18, 2017. The physician prescribed optune which is comprised of an electric field generator, transducer arrays, power supply items, and accessories for 6 months. Preferred treatment start date was ASAP. (*Id.* at 16-17).

In this case, the QIC denied the claim stating the records do not support the device is reasonable and necessary, which is required as outlined in the LCD L34823. (Exh. 1, pp. 1-6). As mentioned above, ALJ's are not bound by the manuals or the LCD's, but they are to give substantial deference to these policies when applicable. (42 C.F.R. § 405.1062). In this case, LCD L34823 does not address newly diagnosed glioblastoma, which indicates that it is not applicable to the Beneficiary's case because the optune device was prescribed for her newly diagnosed glioblastoma. Moreover, pursuant to the Medicare Program Integrity Manual, Ch. 13, an LCD must be based on the peer-reviewed literature, consensus of experts and whether or not the relevant medical community has adopted the technology. The LCD must provide a summary of the evidence considered and a rationale for the determination. LCD L34823 does not reflect consideration of the required elements or provide a rationale. Therefore, because the LCD fails to conform to Medicare Program Integrity Manual, Ch. 13, §13.7.1, it is not entitled to deference.

Furthermore, multiple peer-reviewed published studies demonstrate the safety and efficacy of the optune device. Pursuant to the Journal of the American Medical Association, studies found the addition of Optune to standard chemotherapy treatment "resulted in statistically significant improvement in progression-free survival and overall survival" over patients that were treated with chemotherapy alone. Adding optune to traditional chemotherapy treatment "resulted in statistically significant lower deterioration-free survival in global health status, physical and emotional functioning, pain, and weakness of legs." Additionally, for newly diagnosed glioblastoma, the National Comprehensive Cancer Network guidelines issued a level 1 recommendation, a consensus exists among the experts, based on the highest levels of evidence, that TTFT should be used for glioblastoma. The Data Safety Monitoring Board for the clinical trial for newly diagnosed glioblastoma found the data so compelling, they recommended early termination and allowing patients who were not receiving the treatment to be able to cross over and receive the treatment, and deemed it unethical to withhold it; the Federal Drug Administration agreed. Thus, a consensus exists that published peer-reviewed literature demonstrates the effectiveness of the optune device for newly diagnosed glioblastomas and have shown a significantly improved medical outcome. As a result, the electric stimulation cancer treatment (E0766) was medically reasonable and necessary under section 1862 (a)(1)(A) of the Act and is reimbursable under Medicare Law.

CONCLUSIONS OF LAW

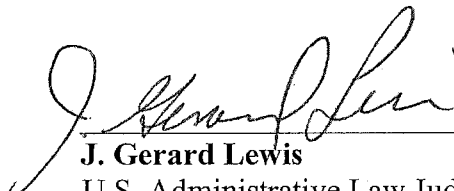
Accordingly, after careful consideration of the evidence, there is sufficient evidence to support Medicare coverage for electric stimulation cancer treatment (E0766), provided to the Beneficiary on September 2, 2017 and February 2, 2018. Therefore, the Appellant is entitled to reimbursement under Medicare Part B.

ORDER

The Medicare Contractor is **DIRECTED** to process the claim in accordance with this decision.

SO ORDERED.

Dated: NOV 14 2018


J. Gerard Lewis
U.S. Administrative Law Judge



Department of Health and Human Services
OFFICE OF MEDICARE HEARINGS AND APPEALS
Kansas City Field Office
Kansas City, Missouri

Appellant:		ALJ Appeal No.: 1-4039359547
Enrollee:		Medicare Part: C
HICN:	****5216A	Before: Bruce MacDougall U.S. Administrative Law Judge
MA Plan:	Blue Cross Blue Shield of North Carolina	

DECISION

After carefully considering the evidence and arguments provided in the record and at the hearing, a **FULLY FAVORABLE** decision is entered for [REDACTED].

PROCEDURAL HISTORY

[REDACTED] is enrolled in Blue Cross Blue Shield of North Carolina, a Part C Medicare Advantage Plan ("the Health Plan"). [REDACTED] submitted a request for pre-approval to the Health Plan for tumor treating fields therapy utilizing an electric stimulation device (HCPCS Code E0766). The Health Plan denied coverage of the tumor treating fields therapy, and Jorge Morales with Novocure appealed on [REDACTED] half. Upon redetermination, the Health Plan once again denied coverage. The Appellant then requested reconsideration from Maximus Federal Services, an Independent Review Entity ("IRE"), and on February 11, 2016, the IRE denied coverage.

On February 22, 2016, the Office of Medicare Hearings and Appeals ("OMHA") received [REDACTED]'s expedited request for an Administrative Law Judge ("ALJ") hearing. On March 24, 2016, a hearing was held before ALJ Bruce MacDougall. [REDACTED] was represented by Novocure, with Sean McGarland and Shawn Dias appearing as witnesses. Attorney at Law Brian Vick represented the Health Plan. Susan Parrish and Dr. Larry Wu provided testimony on its behalf. Exhibits 1 through 5 were admitted into the record. The administrative record is now closed.